

**A STUDY ON CLINICAL DETERMINANTS AND ONE YEAR
FOLLOW-UP OF DEMENTIA AND MILD COGNITIVE
IMPAIRMENT FOLLOWING ISCHEMIC STROKE**

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DM (NEUROLOGY) – BRANCH – I



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CERTIFICATE

This is to certify that the Dissertation entitled, **“CLINICAL DETERMINANTS AND ONE YEAR FOLLOW-UP OF DEMENTIA AND MILD COGNITIVE IMPAIRMENT FOLLOWING ISCHEMIC STROKE”** is the bonafide record work done by Dr.N.Murugapandian, under our guidance and supervision in the Institute of Neurology, Rajiv Gandhi Government General Hospital, Madras Medical College, Chennai, submitted as partial fulfilment for the requirements of D.M. Degree examination Branch I NEUROLOGY, AUGUST 2011, under The Dr.M.G.R. Medical University, Chennai.

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LIST OF ABBREVIATIONS

NCI	-	No Cognitive Impairment
VaMCI	-	Vascular Mild Cognitive Impairment
VaD	-	Vascular Dementia
MCI	-	Mild Cognitive Impairment
CT	-	Computerized Tomogram
MRI	-	Magnetic Resonance Imaging
MMSE	-	Mini Mental Status Examination
BNT	-	Boston Naming Test
RAVLT	-	Rey Auditory Verbal Learning Test
BI	-	Barthel Index
ADL	-	Activities of Daily Living
ACA	-	Anterior Cerebral Artery
MCA	-	Middle Cerebral Artery
PCA	-	Posterior Cerebral Artery

INTRODUCTION

Cognitive impairment due to cerebrovascular disease is termed “Vascular Cognitive Impairment” and forms a spectrum that includes Vascular Dementia and milder forms of cognitive impairment referred to as Vascular Mild Cognitive Impairment.[1] While Vascular Dementia is the second most common cause of dementia, the milder form Vascular Mild Cognitive Impairment is much more common. Nearly half of individuals with Vascular Mild Cognitive Impairment convert to dementia after five years.[2] Vascular cognitive disorders are poised to become the silent epidemic of the 21st century and contribute significantly to mortality, disability, and decreased quality of life.[3]

It is now clear that Vascular Cognitive Impairment is not a single entity, but represents a complex neurological disorder that occurs as a result of interaction between vascular risk factors and brain parenchymal changes such as macro and micro infarcts, haemorrhages, white matter changes, and brain atrophy occurring in an ageing brain.

Factors that determine progression of milder form Vascular Mild Cognitive Impairment to dementia are not well understood. Since Vascular Cognitive Impairment is amenable to prevention and treatment, there is a pressing need to identify factors that protect or predispose to it.

Dementia is a common sequelae of stroke with a frequency ranging from 16% to 32%. [4–5] In a more recent epidemiological study, the 10-year risk of dementia after stroke was estimated at 19.3%, compared to 11.0% in non-stroke controls. [6] This twofold increase in dementia following stroke is in contrast with a nine fold increase reported in some previous studies. [7] The large variation in rates is accounted for by variations in the populations studied as well as the criteria used for the diagnosis of dementia. As the definition of vascular dementia is currently being refined, [8] it is timely that these studies be revisited. One aspect of this reassessment is the consideration of vascular mild cognitive impairment in stroke patients, which has thus far received little attention.

Most studies on post stroke cognitive impairment have focused on dementia. Bowler and Hachinski a decade ago made warnings about the limitations of the diagnostic category of vascular dementia and coined the term vascular cognitive impairment to refer to any cognitive impairment related to cerebrovascular disease. Detection of cognitive impairment has two difficulties: a neuropsychologic battery fitted to the vascular cognitive impairment profile is yet to be established and limits from normal cognition are still undefined. Also, the evidence of the vascular origin of cognitive impairment is difficult to ascertain.

REVIEW OF LITREATURE

DEFINITIONS

Vascular dementia: Vascular dementia is the loss of cognitive functions to a degree that interferes with Activities of Daily Livings, resulting from ischemic or hemorrhagic cerebrovascular disease or from cardiovascular or circulatory disturbances that injure brain regions that are important for memory, cognition, and behaviour. [9] Vascular dementia is the second most common form of dementia after Alzheimer's disease, accounting for approximately 20% of dementia cases worldwide.

Globally, Vascular dementia is more common in men, especially before age 75—in contrast with Alzheimer's disease that predominates in women—and is more prevalent in populations that are affected by cerebral small-vessel disease, such as Asians, Blacks, and Hispanics. In keeping with the predictions of increasing burden of stroke and heart disease in the near future, Vascular dementia will probably become the most common cause of senile dementia, both by itself and as a contributor to other degenerative dementias.[10]

Vascular mild cognitive impairment: Vascular mild cognitive impairment is a recently coined term to signify any degree of cognitive loss caused by cerebrovascular disease, including vascular dementia.

However, by analogy with mild cognitive impairment (MCI) resulting from Alzheimer's disease, the term Vascular Cognitive Impairment is better reserved for patients with risk factors for cerebrovascular disease and some degree of cognitive loss short of dementia.

Intrinsic to the Vascular Cognitive Impairment concept is the hope that appropriate prevention and treatment of cerebrovascular disease can prevent Vascular dementia development. Although this is an appealing undertaking, there have been difficulties in providing a strict definition of Vascular Cognitive Impairment and operational diagnostic criteria. The concept of Vascular Cognitive Impairment suffers from the same problems once criticized in Vascular dementia ; i.e., the notion is too wide and too vague for a precise operative definition. Furthermore, as demonstrated in the Canadian Study on Health and Aging, [11] some patients with a diagnosis of Vascular Cognitive Impairment no dementia improved with time, indicating that progression from Vascular Cognitive Impairment to Vascular dementia may not always be a unidirectional pathway. There is growing evidence that preventive measures to decrease the vascular burden on the brain may also decrease Vascular dementia, as well as Alzheimer's disease.

Mixed dementia: The boundaries between Vascular dementia and Alzheimer's disease recently have become indistinct. The belief that CVD may lead to cognitive decline and dementia in the elderly has been around since 1672, when Thomas Willis first described cases of postapoplectic dementia. Less well recognized is that silent strokes and incomplete white matter ischemia—documented by modern brain imaging—are also strongly associated with cognitive loss, behavioural changes, and Vascular dementia .

During most of the past two centuries, it was widely held that atherosclerotic dementia was the sole cause of senile dementia. It was only in the 1980s that Alzheimer's disease was declared the most common form of dementia in the elderly. However, most elderly patients with dementia who are autopsied will have amyloid plaques and neurofibrillary tangles, the typical brain lesions of Alzheimer's disease, localized in the hippocampal regions (Braak Stages I–III), coexisting with cerebrovascular lesions, such as large and small strokes, hemorrhages, arteriolosclerosis, lacunes, microinfarcts, and ischemic leukoencephalopathy.

Cerebrovascular disease is required to “amplify” the clinical expression of Alzheimer's disease pathology beyond the stage of

amnesic MCI (Braak Stage III). This explains why almost 20% of cases pathologically defined by Consortium to Establish a Registry for Alzheimer Disease (CERAD) criteria as Alzheimer's disease do not have clinical dementia. Conversely, more than half of the octogenarians without dementia meet CERAD criteria for pathologically confirmed Alzheimer's disease. On the other hand, Hénon and colleagues,[12] have also shown that in patients with bonafide postapoplectic Vascular dementia , pre-existing amnesic deficits occurred in 16% of cases, suggesting that the underlying Alzheimer's disease had not progressed beyond Stage III, which is clearly insufficient to produce clinical dementia. Evidence from the Nun Study also concluded that lacunes increase more than 20 times the risk of clinical expression of dementia at early Braak stages that are insufficient to produce dementia. Moreover, in pathologically confirmed cases of “mixed” dementia (Alzheimer's disease +Cerebrovascular Disease, Alzheimer's disease +Vascular dementia), there is a significant inverse relationship between the severity of cerebrovascular disease and Braak stage. In all these patients, Vascular dementia is the defining cause of the dementia.

In addition, population-based studies have shown that silent lacunes are extremely common in the elderly. Longstreth et al. showed the presence of one or more silent lacunes in approximately one fourth of

the 3,660 participants in the Cardiovascular Health Study (CHS) aged 65 and older that underwent cerebral magnetic resonance imaging (MRI). Recently, in the Rotterdam cohort, Vermeer et al. demonstrated that the presence of lacunes, particularly in the thalamus, more than doubled the risk of dementia (hazard ratio = 2.26, 95% CI, 1.09–4.70). Small-vessel disease may be the most common mechanism to convert from MCI into Alzheimer's disease in persons over the age of 70 years.

WHEN TO SUSPECT VASCULAR COGNITIVE IMPAIRMENT

Typically, patients with vascular cognitive impairment are not found in memory disorder clinics, because memory loss is a less prominent manifestation of this syndrome. This must be considered when extrapolating figures of dementia prevalence from hospital- or office-based data. This also explains the alleged rarity of vascular cognitive impairment in neuropathologically examined specimens from brain banks of Alzheimer's Disease clinics. Primary care settings are the main referral source of patients with vascular cognitive impairment. The vascular cognitive impairment should be suspected in any patients presenting with cognitive impairment and various risk factors (Table.1)

Table.1. Risk Factors for Vascular Dementia

1. Advanced age	10.Hyperfibrinogenemia
2. Long-term, untreated arterial	11.Atrial fibrillation
3. hypertension	12.Other cardiac arrhythmias
4. Isolated systolic hypertension	13.Complicated stroke
5. in the elderly	14.Recurrent stroke
6. Diabetes mellitus	15.Orthostatic hypotension
7. Cigarette smoking	16.Obstructive sleep apnea
8. Hyperlipidemia	17.Major surgery in the elderly
9. Hyperhomocysteinemia	18.Coronary artery graft Surgery

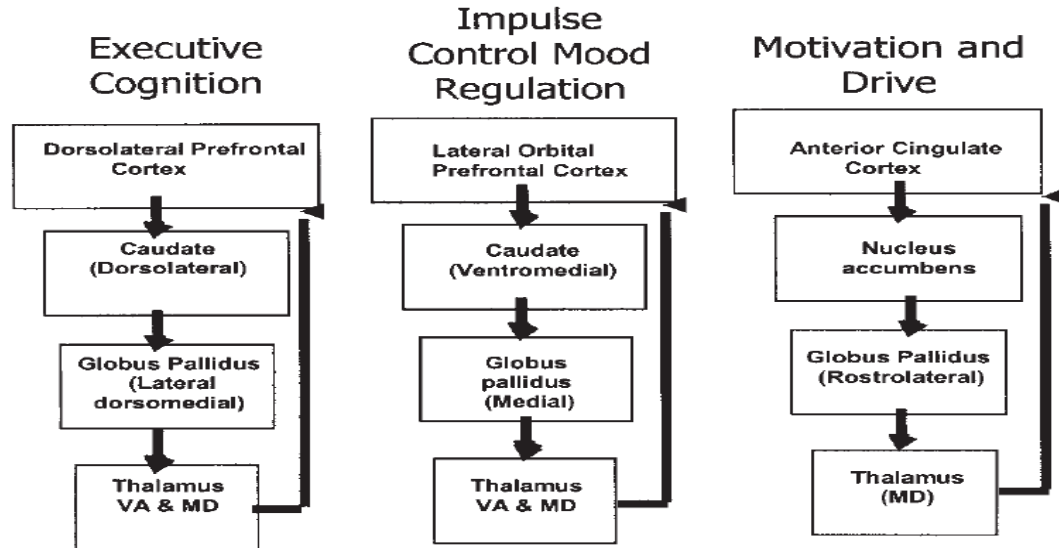
Cortical and Subcortical Dementias: Clinicians divide the dementia syndrome into two main types, cortical and subcortical, according to the clinical features and the pattern of neuropsychological impairment. The prototypical cortical dementia is Alzheimer's Disease that manifests preponderantly with early and severe memory disturbances, aphasia, agnosia, and apraxia resulting from lesions involving posterior cortical association regions. In sharp contrast, Vascular Dementia manifestations, a typical subcortical dementia, include slowing of cognition and motor

function owing to executive control, along with prominent alterations of gait, speech, affect, and mood. The manifestations mentioned result from the interruption by ischemic lesions of frontal cortico-subcortical circuits (see Fig. 1) for executive control of memory, language, mood, constructional skills, motivation, and socially responsive behaviors.

THE NEUROPATHOLOGIC SUBSTRATES OF VASCULAR-ISCHEMIC DEMENTIA

Fundamental pathological lesions in Vascular Cognitive Impairment consist of atherosclerosis with or without thrombosis/thromboembolism of extracerebral and intracerebral arteries, intracerebral microangiopathies—arteriosclerotic, hyalinotic, inflammatory, and amyloid-related—often combined with systemic factors that may produce small and large infarcts and several forms of white matter degeneration. The extent and location of cerebrovascular lesions and destroyed tissues, which differ considerably from case to case, multiplicity, and bilateral occurrence, are the most important factors underlying cognitive impairment.

Figure 1. Frontal-subcortical-thalamic circuits



One of the most controversial and incompletely understood issues is the degree to which vascular pathology contributes to dementia. Complicating the postmortem Vascular Cognitive Impairment diagnosis are other pathologic entities coexisting with vascular lesions that could lead to cognitive decline. Many of these can be found at postmortem examination, particularly in multimorbid elderly subjects.

However, it should be emphasized that the presence of cerebrovascular lesions at autopsy does not prove that they cause cognitive decline, underscoring that thorough clinicopathologic correlation is essential to establish a definite diagnosis. Although several class I and II studies that compared clinical diagnosis and neuropathologic findings in reference cohorts, which are similar to

population-based studies, reported low sensitivity and specificity for the currently used clinical diagnostic Vascular Cognitive Impairment criteria with variable interrater reliability. According to recent clinicopathologic studies, The Mayo Clinic criteria (temporal relationship between stroke and dementia or worsening or bilateral infarctions in specified locations) had 75% sensitivity and 81% specificity for pure Vascular Dementia.

Because the criteria chosen to diagnose Vascular Dementia will influence estimates on its incidence and prevalence, as well as its recognition and treatment, new research criteria (e.g., for subcortical Vascular Dementia) have been proposed, and the need for prospective clinicopathologic correlation studies has been emphasized. These criteria can only be established at autopsy in patients who have been thoroughly and longitudinally evaluated before death and who do not have other causes of dementia.

Vascular Cognitive Impairment is related to a variety of pathologic lesions, the clinical significance of which and their relation to Alzheimer's Disease and other age-related changes of the brain (e.g., subcortical white matter lesions) remain controversial. However, we are not aware of any validation study of the neuropathologic Vascular Cognitive Impairment criteria.

Although causal relationships between certain cerebrovascular lesions and dementia evade strict classifications and no classification of brain lesions causing cognitive impairment is ideal, the major cerebrovascular lesions associated with cognitive impairment are summarized below.

Major Morphological Types of Vascular Dementia:

1. Classical multiinfarct encephalopathy (MIE) Multiple large (sub/territorial) infarcts in cortex and white matter/basal ganglia in territories of large cerebral arteries, MCA, MCA plus PCA; involving left or both hemispheres.

2. Strategic infarct dementia (SID) Small or medium-sized infarcts/ischemic scars in functionally important brain regions: thalamus; hippocampus (PCA), basal forebrain angular gyrus (ACA), bilaterally or dominant hemispheres.

3. Microangiopathic (small vessel infarct) dementia (SMVA)

a. Subcortical arteriosclerotic leukoencephalopathy Binswanger (SAE) Multiple small infarcts in basal ganglia plus white matter with preservation of cortex

b. Multilacunar state Multiple microinfarcts (scars up to 1.5 cm); basal ganglia, hemispherical white matter, pontine basis

Multiple cortico-subcortical microinfarctions (mixed encephalopathies)

c. Granular cortical atrophy Multiple small scars within border zones ACA MCA in one/both hemispheres

4. Subcortical microvascular leukoencephalopathy (acquired/genetically determined)

5. Gliosis or hippocampal sclerosis

6. Inflammatory angiopathy and other mechanisms

Dementia Associated With Cerebrovascular Disease:

A. Multifocal/diffuse disease

1. Multiple atherosclerotic/watershed infarcts (large artery/border zone territories)

2. Anti-PL-related ischemia

3. “Granular atrophy” of cortex (multifocal cortical microinfarcts)

4. Multiple lacunar infarcts (resulting from microvascular disease or microatheroma)

5. Binswanger subcortical leukoencephalopathy (BSLE)

6. CADASIL

7. Angiitis

8. Cerebral amyloid angiopathy (CAA) plus/minus infarcts, hemorrhages (Alzheimer's Disease variant?)—Familial forms, including Dutch, Icelandic, British

9. Miscellaneous angiopathies (FMD, Moyamoya)

10. Cortical laminar necrosis (post-cardiac arrest, hypotension)

11. Extreme dilatation/enlargement of brain parenchymal perivascular spaces

B. Focal disease/strategically placed infarcts

1. Mesial temporal (including hippocampal) infarcts/ischemia/sclerosis

2. Caudate and thalamic infarcts (especially DM nucleus, bilateral damage)

3. Frontal-cingulate infarcts (ACA territory)

4. Angular gyrus infarct (dominant cerebral hemisphere)

THE COGNITIVE PROFILE OF VASCULAR DEMENTIA

A review of the literature on neuropsychological functioning in Vascular Dementia makes clear that several, if not all, cognitive domains are affected when compared to normative data or normal control samples. To illustrate this point, Figure.2 depicts neurocognitive performances of patients with mild and severe Vascular Dementia. As the figure shows, the samples performed in the impaired range across all domains. Thus, the question arises whether there is a unique profile or cognitive aspect of Vascular Dementia.

Obviously, the nature and location of vascular neuropathology can impact cognitive functioning in the case of classic stroke syndromes. However, regarding small-vessel disease, it has been argued that impairment in executive functioning and relative preservation of recognition memory are necessary cognitive criteria for Vascular Dementia.[13] The executive deficits are a hallmark symptom of Vascular Dementia, which appear regardless of the presence or absence of cognitive dysfunction in other domains. An analogy can be drawn to the conceptualization of Alzheimer's Disease, as memory-encoding difficulties have been referred to as the sine qua non of Alzheimer's Disease. Although memory difficulties are not the only clinical

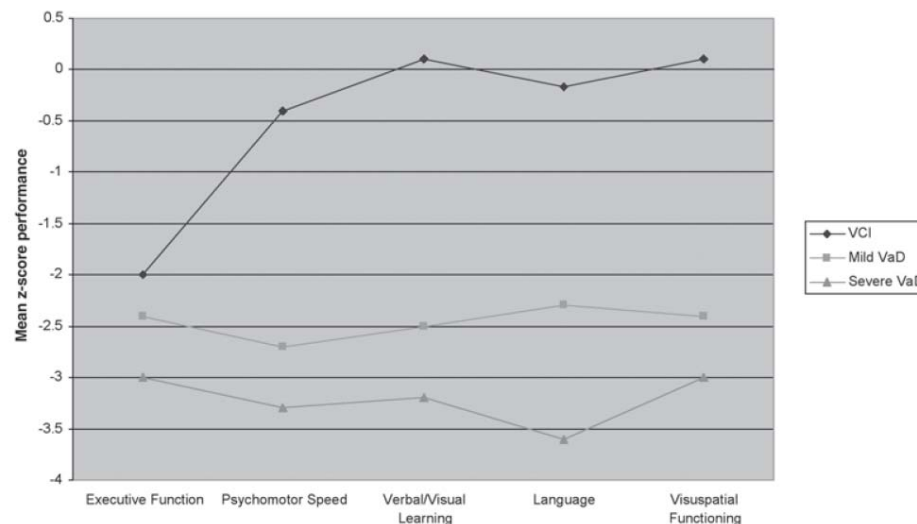
manifestation of Alzheimer's Disease, it is widely believed that for most, but certainly not all, cases of Alzheimer's Disease, memory dysfunction is an early and prominent symptom that is expressed throughout the course of the disease. With time, additional cognitive symptoms become apparent (e.g., deficits in language, praxis, construction, and executive function); however, memory disturbance is a cardinal feature of the disease. Similarly, many believe that executive deficits represent a common manifestation of Vascular Dementia.

The neuroanatomic underpinnings of executive dysfunction in Vascular Dementia have traditionally been attributed to disruption of the frontal subcortical circuits initially outlined by Alexander and colleagues, who described a series of parallel but functionally segregated circuits that link subcortical structures to the frontal lobes. Perhaps the most relevant circuit to Vascular Dementia is that involving the dorsolateral prefrontal cortex, as the dysexecutive syndrome that emerges from damage to this pathway is the most common clinical presentation in Vascular Dementia. Indeed, there is some evidence that white matter disease in subcortical structures involved in this pathway (i.e., thalamus and basal ganglia) is associated with executive dysfunction in patients with Vascular Dementia.

INDIAN PERSPECTIVE

In terms of population, India ranks second only to China. Recent rapid socioeconomic changes have led to a concomitant change in people's lifestyle, leading to work-related stress and altered food habits, raising the risk of hypertension. Those factors, coupled with an increase in the average life expectancy, are expected to have an impact on the occurrence of stroke as well as stroke related complications in India.

Figure. 2. Neurocognitive performances of patients with mild and severe vascular dementia in relation to hypothetical performances of patients with vascular cognitive impairment



Vascular cognitive impairment is a problem close to home. Developing countries have a rapidly ageing population and it is projected that 71% of dementia cases will be in the developing world. Vascular Dementia is the second most common cause of dementia accounting for 39% of cases,[14] and hence, absolute numbers of Vascular Dementia, is high in India.[15]

Cardiovascular disease burden is high in developing countries including India and has been attributed to the increasing incidence of atherosclerotic diseases, perhaps due to urbanization, epidemiologic transition and higher risk factor levels, the relatively early age at which they manifest, the large sizes of the population, and the high proportion of individuals who are young adults or middle-aged in these countries.[16] Vascular risk factors has been demonstrated to be strongly associated with MCI in an epidemiologic study from Kolkata. Higher prevalence of vascular risk factors in India is likely to increase burden of Vascular Dementia and Vascular Mild Cognitive Impairment.

Stroke, the overt manifestation of cerebrovascular disease is one of the most important risk factors for Vascular Dementia. Stroke burden is increasing rapidly in developing countries (124% and 107% increases in stroke mortality among men and women in developing countries versus

78% and 56% increases, respectively, in the developed countries). Studies have consistently shown that up to 64% of persons who have experienced a stroke have some degree of cognitive impairment[17] with up to a third developing frank dementia.[18] In a hospital-based study from Hyderabad, of 123 consecutive patients from the Stroke registry evaluated a minimum of 3 months after stroke, 91 (74%) were found to have cognitive impairment- 31% with Vascular Dementia and 43% with Vascular Mild Cognitive Impairment. A longitudinal follow-up of 50% of the group over a mean period of 13 months demonstrated that all patients with dementia at baseline continued to have dementia at follow-up and none of the cognitively normal patients worsened. Course of Vascular Mild Cognitive Impairment was variable-seven patients reverted to normal and one patient progressed to dementia.[19]

Inadequate resources and low awareness coupled with growing numbers of patients with Vascular Mild Cognitive Impairment make it a problem that needs urgent attention on a priority basis.

DIAGNOSIS

The diagnosis of vascular cognitive impairment requires establishing the presence of cognitive impairment and its association with cerebrovascular disease. Identifying the presence and impact of cognitive

impairment involves the following steps: reporting of subjective symptoms, objective confirmation by neuropsychological and behavioural assessment, determination of severity of cognitive decline, and its functional impact on Activities of Daily Living. Cerebrovascular disease can be established by the clinical history of a stroke and the presence of focal neurological deficits corroborated by brain imaging. The mechanism underlying the stroke can be identified by the use of appropriate investigations, including Electrocardiogram, 2D Echocardiogram, extracranial and intracranial vascular imaging, and hematological investigations. The association between stroke and cognitive impairment is thought to be substantiated by a temporal relationship between the two and location of infarct in a region appropriate for cognitive impairment.

Clearly a great degree of variability exists in the method of establishing all these features. This difficulty is evident from the various criteria that have been proposed for the diagnosis of Vascular Dementia. Majority of them have been devised based on consensus rather than clinical data. The Hachinski ischemic score (Table.2), a simple clinical tool that performs well in the differentiation between Alzheimer's dementia and multi-infarct dementia, the purpose for which it was originally designed, but mixed dementia remains difficult. [20]

The four sets of criteria (Table.3 &4) currently being used in clinical practice and research include International Classification of Diseases-10 (ICD-10), Diagnostic and Statistic Manual-IV (DSM-IV), State of California Alzheimer's Disease Diagnostic and Treatment Centres (ADDTC), and the National Institute for Neurological Disorders and Stroke-Association Internationale pour la Recherche et a'Enseignement en Neurosciences (NINDS-AIREN) criteria. [21],[22] Cognitive impairment and presence of significant cerebrovascular disease are common to all criteria, but the method of establishing their presence and the causal relationship between them is variable. Studies evaluating the validity and reliability of these criteria have demonstrated that the existing criteria are not sufficiently sensitive, use different definitions of dementia, and are not easily interchangeable. [23]

In an attempt to resolve this controversy, an attempt has been made to simplify the classification system based on clinical and imaging features. Vascular cognitive impairment, classified on the basis of clinical and imaging features into Vascular cognitive impairment without dementia, Vascular Dementia and mixed degenerative/ Vascular Dementia was found to be useful in a large hospital-based cohort of patients. [24]

In an attempt to harmonise methodology to identify and describe individuals with Vascular Cognitive Impairment, particularly in the early stages, the National Institute for Neurological Disorders and Stroke (NINDS) and the Canadian Stroke Network (CSN) developed common standards in clinical diagnosis, epidemiology, brain imaging, neuropathology, experimental models, genetics, and clinical trials to recommend minimum, common, clinical, and research standards for the description and study of vascular cognitive impairment. [25] Using the same standards was thought to help identify individuals in the early stages of cognitive impairment, make studies comparable, and integrate knowledge, thereby accelerating the pace of progress of understanding, preventing and treating Vascular Cognitive Impairment.

Table.2 . Hachinski Ischemia Score

Abrupt onset	2
Stepwise deterioration	1
Fluctuating course	2
Nocturnal confusion	1
Relative preservation of personality	1
Depression	1
Somatic complaints	1
Emotional incontinence	1
History of hypertension	1

History of strokes	2
Evidence of associated atherosclerosis	1
Focal neurological symptoms	2
Focal neurological signs	2
Total score:	---

Table.3. DSM-IV Criteria for the Diagnosis of Vascular Dementia

1.	<p>The development of multiple cognitive deficits manifested by both memory impairment and one or more of the following cognitive disturbances:</p> <ul style="list-style-type: none"> a. Aphasia (language disturbance). b. Apraxia (impaired ability to carry out motor activities despite intact motor function). c. Agnosia (failure to recognize objects despite intact sensory function). d. Disturbance in executive functioning
2.	<p>The cognitive deficits in criteria 1a and 1b each cause significant impairment in social or occupational functioning and represent a significant decline from a previous level of functioning</p>
3.	<p>Focal neurological signs and symptoms (e.g., exaggeration of deep tendon reflexes, extensor plantar response, pseudobulbar palsy, gait</p>

	abnormalities, weakness of an extremity), or laboratory evidence indicative of cerebrovascular disease (e.g., multiple infarctions involving cortex and underlying white matter) that are judged to be etiologically related to the disturbance
4.	The deficits do not occur exclusively during the course of a delirium

Table.4. NINDS-AIREN Criteria for the Diagnosis of Vascular Dementia

1.	<p>The criteria for the clinical diagnosis of probable vascular dementia include all of the following:</p> <p>A. Dementia, defined by cognitive decline from a previously higher level of functioning and manifested by impairment of memory and of two or more cognitive domains (orientation, attention, language, visuospatial functions, executive functions, motor control, and praxis), preferably established by clinical examination and documented by neuropsychological testing; deficits should be severe enough to interfere with ADL not because of physical effects of stroke alone.</p> <p>Exclusion criteria: cases with disturbance of consciousness, delirium, psychosis, severe aphasia, or major sensorimotor impairment precluding neuropsychological testing. Also excluded are systemic disorders or other brain diseases (such as Alzheimer's disease) that in and of themselves could account for deficits in memory and cognition.</p>
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	<p>B. Cerebrovascular disease, defined by the presence of focal signs on neurological examination, such as hemiparesis, lower facial weakness, Babinski sign, sensory deficit, hemianopia, and dysarthria consistent with stroke (with or without history of stroke), and evidence of relevant cerebrovascular disease by brain imaging (computed tomography or magnetic resonance imaging [MRI]) including multiple large-vessel infarcts or a single strategically placed infarct (angular gyrus, thalamus, basal forebrain, or posterior cerebral artery or anterior cerebral artery territories), as well as multiple basal ganglia and white matter lacunes, or extensive periventricular white matter lesions, or combinations thereof.</p> <p>C. A relationship between the above two disorders, manifested or inferred by the presence of one or more of the following:</p> <ul style="list-style-type: none"> a. Onset of dementia within 3 months following a recognized stroke. b. Abrupt deterioration in cognitive functions. c. Fluctuating, stepwise progression of cognitive deficits
2	<p>Clinical features consistent with the diagnosis of probable vascular dementia include the following:</p> <ul style="list-style-type: none"> A. Early presence of gait disturbance. B. History of unsteadiness and frequent, unprovoked falls. C. Early urinary frequency, urgency, and other urinary symptoms not explained by urological disease.

	<p>D. Pseudobulbar palsy.</p> <p>E. Personality and mood changes, abulia, depression, emotional incontinence, or other subcortical deficits including psychomotor retardation and abnormal executive function</p>
3	<p>Features that make the diagnosis of vascular dementia uncertain or unlikely include the following:</p> <p>A. Early onset of memory deficit and progressive worsening of memory deficit and progressive worsening of memory and other cognitive functions, such as language (transcortical sensory aphasia), motor skills (apraxia), and perception (agnosia), in the absence of corresponding focal lesions on brain imaging.</p> <p>B. Absence of focal neurological signs, other than cognitive disturbance.</p> <p>C. Absence of cerebrovascular lesions on brain CT or MRI</p>
4	<p>Clinical diagnosis of possible vascular dementia may be made in the presence of dementia (section I-A) with focal neurological signs in patients in whom brain imaging studies to confirm definite CVD are missing; or</p> <p>in the absence of clear temporal relationship between dementia and stroke; or in patients with subtle onset and variable course (plateau or improvement) of cognitive deficits and evidence of relevant CVD</p>

5	<p>Criteria for diagnosis of definite vascular dementia are:</p> <p>A. Clinical criteria for probable vascular dementia.</p> <p>B. Histopathological evidence of CVD obtained from biopsy or autopsy.</p> <p>C. Absence of neurofibrillary tangles and neuritic plaques exceeding those expected for age.</p> <p>D. Absence of other clinical or pathological evidence for dementia</p>
6	<p>Classification of vascular dementia for research purposes may be made based on clinical, radiological, and neuropathological features, for subcategories or defined conditions, such as cortical vascular dementia,</p> <p>subcortical vascular dementia, Binswanger's disease, and thalamic dementia</p>

All of these criteria sets have very different specificities and sensitivities. Although the ADDTC criteria might be most useful in clinical settings, and the NINDS-AIREN criteria the most useful in research settings, the lack of comparability between diagnostic criteria is a barrier for both of these criteria. OUTCOME

Vascular dementia shortens life expectancy. A 5-year follow-up study of incident dementia cases[26] found that mortality risk was 3.3-times higher for vascular dementia compared with non-demented people.

Nearly half of elderly with MCI due to vascular disease converted to dementia after 5 years in the Canadian Study of Health and Aging. Further, a follow-up study of people with Vascular Cognitive Impairment, Alzheimer's Disease and 'No cognitive impairment', showed that most people with Vascular Cognitive Impairment showed readily detectable progression by 30 months and depressive symptoms and impaired judgement progressed more commonly in patients with Vascular Cognitive Impairment.[27] In a longitudinal study of Vascular Dementia due to subcortical lacunar infarcts, progressive cognitive decline was determined mainly by the occurrence of new vascular episodes and severity of the cognitive impairment at baseline, providing evidence that ongoing vascular insult is responsible for progression of disease.[28]

TREATMENT:

Based on the various pathophysiological mechanisms proposed to underlie Vascular Cognitive Impairment, a wide range of management strategies have been tried to treat Vascular Cognitive Impairment, including control of risk factors, treating stroke mechanism, treatment of cognitive disorder, management of behavioral symptoms, cognitive retraining, and caregiver support. Attempts to reverse or delay

progression of cognitive impairment due to cerebrovascular disease by recent studies have given grounds for hope of treatment of Vascular Dementia.

Decreased incidence of dementia associated with antihypertensive treatment using nitrendipine and perindopril has been demonstrated.[29,30] The Syst-Eur study found that a calcium-channel blocker-based regimen for the treatment of hypertension reduced the incidence of dementia by 50% in older patients with isolated systolic hypertension studies suggest that the use of lipid-lowering agents lowers the risk of dementia and protects against cognitive decline.[31] Recent evidence suggests that prevention of Vascular Cognitive Impairment may be possible through physical activity.[32,33]

In a randomised trial of 325 mg/day aspirin (versus no aspirin) conducted on multi-infarct dementia patients, the group of aspirin patients showed significantly higher cognitive scores than the untreated group.[34] The use of acetylcholinesterase inhibitors is based on the demonstration of existence of cholinergic deficits in pure Vascular Dementia. Donepezil tested in two double-blind, placebo-controlled trials on patients diagnosed with possible or probable Vascular Dementia showed significant improvement in cognition (ADAS-cog, MMSE) and

global functioning scores. [35] Galantamine, Rivastigmine, and Memantine have also demonstrated improvement in cognition and caregiver.[36,37]

BEST PRACTICE RECOMMENDATION: VASCULAR COGNITIVE IMPAIRMENT AND DEMENTIA[38]

All patients with vascular risk factors and those with clinically evident stroke or transient ischemic attack should be considered at high risk for vascular cognitive impairment.

Patients considered at high risk for cognitive and perceptual impairment are those with vascular risk factors such as hypertension, age > 65, hyperlipidemia, diabetes, clinical stroke, neuroimaging findings of covert stroke or white matter disease, damage to other target organs, and/or those patients with cognitive or functional changes that are clinically evident or reported during history-taking.

Assessment

- ✓ 1.All patients described above should be screened for cognitive impairment using a validated screening tool [Evidence Level B] ("Clinical guidelines for acute stroke management 2007," 2007; "Stroke Canada Optimization of Rehabilitation through Evidence [SCORE]," 2007).

- ✓ 2.Screening to investigate a person's cognitive status should address the following domains: arousal, alertness, attention, orientation, memory, language, agnosia, visuospatial/perceptual function, praxis and executive functions such as insight, judgment, social cognition, problem- solving, abstract reasoning, initiation, planning and, organization [Evidence Level C].
- ✓ 3.The Montreal Cognitive Assessment is considered more sensitive to cognitive impairment than the Mini Mental Status Exam in patients with vascular cognitive impairment. Its use is recommended when vascular cognitive impairment is suspected [Evidence Level B] (Chertkow, 2007). Additional validation is needed for the Montreal Cognitive Assessment as well as other potential screening instruments such as the 5-minute protocol from the Vascular Cognitive Impairment Harmonization recommendations.
- ✓ 4.Patients should also be screened for depression, since depression has been found to contribute to cognitive impairment in stroke patients. A validated screening tool for depression should be used [Evidence Level B] (Chertkow, 2007).
- ✓ 5.Persons who have cognitive impairment detected on a screening test should receive additional cognitive and/or neuropsychologic assessments as appropriate to further guide management [Evidence Level B] (Chertkow, 2007).

Timing

- ✓ 1. All patients considered at high risk for cognitive impairment should be assessed periodically as indicated by severity of clinical presentation, history and/or imaging abnormalities to identify cognitive, perceptual deficits, depression, delirium and/or changes in function [Evidence Level C].
- ✓ 2. Those who have suffered a transient ischemic attack or stroke should have a screening assessment and, where indicated, a more in-depth assessment of cognitive and perceptual status at various transition points throughout the continuum of stroke care [Evidence Level C]. Transition points may include:
 - a. During presentation to emergency when cognitive, perceptual or functional concerns are noted
 - b. Upon admission to acute care, particularly if any evidence of delirium is noted
 - c. Upon discharge home from acute care or during early rehabilitation if transferred to inpatient rehabilitation setting
 - d. Periodically during in-patient rehabilitation stage according to client progress and to assist with discharge planning

- e. Periodically following discharge to the community by the most appropriate community health care provider according to client's needs, progress and current goals

Management

- ✓ 1. All vascular risk factors should be managed aggressively to achieve optimal control [Evidence Level A] (Chertkow, 2007).
- ✓ 2. Patients who demonstrate cognitive impairments in the screening process should be referred to a health care professional with specific expertise in this area for additional cognitive, perceptual and/or functional assessment to determine the severity of impairment and impact of deficits on function and safety in activities of daily living and instrumental activities of daily living, and to implement appropriate remedial, compensatory and/or adaptive intervention strategies [Evidence Level B] (Chertkow, 2007). A team approach is recommended, and health care professionals may include an occupational therapist, neuropsychologist, psychiatrist, neurologist, geriatrician, speech–language pathologist or social worker.
- ✓ 3. An individualized, client-centred approach should be considered to facilitate resumption of desired activities such as return to work, leisure, driving, volunteer participation, financial management,

home management and other instrumental activities of daily living [Evidence Level C] (Chertkow, 2007).

- ✓ 4. Intervention strategies including rehabilitation should be tailored according to the cognitive impairments and functional limitations as well as remaining cognitive abilities, as identified through in-depth assessment and developed in relation to patients' and caregivers' needs and goals [Evidence Level B] .
- ✓ 5. Strategic or compensatory training appears to be effective in the treatment of apraxia post stroke and should be considered [Evidence Level A] (Teasell, et al. 2007). The evidence for the effectiveness of specific interventions for cognitive impairment in stroke is limited and requires more research. Attention training may have a positive effect on specific, targeted outcomes and should be implemented with appropriate patients [Evidence Level C] (Teasell, et al., 2007). Compensatory strategies can be used to improve memory outcomes [Evidence Level C] (Teasell, et al., 2007).
- ✓ 6. Patients with evidence of depression or anxiety on screening should be referred and managed by an appropriate mental health professional [Evidence Level C].

✓ 7. Pharmacotherapy:

- a. •Patients with evidence of vascular cognitive impairment should be referred to a physician with expertise in vascular cognitive impairment for further assessment and recommendations regarding pharmacotherapy [Evidence Level C].
- b. •Cholinesterase inhibitors should be considered for management of vascular cognitive impairment diagnosed using the National Institute of Neurological Disorders and Stroke (NINDS) — Association Internationale pour la Recherche et l'Enseignement en Neurosciences (AIREN) diagnostic criteria [Evidence Level B] (Chertkow, 2007).
- c. •There is fair evidence of small magnitude benefits for galantamine on cognition function and behaviour in mixed Alzheimer and cerebrovascular disease. Galantamine can be considered a treatment option for mixed Alzheimer and cerebrovascular disease [Evidence Level B] (Chertkow, 2007).
- d. •There is fair evidence of small magnitude benefits for donepezil in cognitive and global outcomes, with less robust benefits on functional measures. Donepezil can be considered a treatment option for vascular dementia [Evidence Level B] (Chertkow, 2007).

Levels of Evidence

Grade	Criteria
A	Strong recommendation. Evidence from randomized controlled trials or meta-analyses of randomized controlled trials. Desirable effects clearly outweigh undesirable effects, or vice versa.
B	Single randomized controlled trial or well-designed observational study with strong evidence; or well-designed cohort or case–control analytic study; or multiple time series or dramatic results of uncontrolled experiment. Desirable effects closely balanced with undesirable effects.
C	At least one well-designed, nonexperimental descriptive study or expert committee reports, opinions and/or experience of respected authorities, including consensus from development and/or reviewer groups.

CONCLUSIONS:

Vascular risk factors and cerebrovascular disease are now recognized to account for a major proportion of cognitive disorders, including degenerative dementias. Emphasis has shifted from diagnosis of Vascular Dementia based on restrictive criteria to include a broader spectrum of disease Vascular Cognitive Impairment that includes mixed dementia and cognitive impairment with no dementia. Control of vascular risk factors and treatment of milder forms of disease need to form the focus of preventive strategies. Variability exists in burden of Vascular Dementia, its risk factors, subtypes and outcome in different countries and ethnic populations and elucidating reasons for these differences will help in reducing burden of cognitive impairment due to cerebrovascular disease globally.

AIMS AND OBJECTIVE

To investigate the frequency and clinical determinants of dementia and mild cognitive impairment following ischemic stroke. The age, education, pre-stroke cognitive decline, stroke volume, number of strokes, baseline cerebral atrophy, non-infarct white matter pathology, and risk factors for atherosclerosis were addressed specifically. The one year follow-up was done to assess the prognosis.

MATERIALS AND METHODS

Subjects were ischemic stroke patients referred to neurology outpatient clinic of Madras Medical College during January 2009 to March 2011.

Inclusion criteria

100 consecutive patients aged ≥ 40 years with the diagnosis of ischemic stroke within previous 2 - 3 months.

Exclusion criteria

1. Prestroke dementia
2. No baseline CT
3. Neurological disorder other than the qualifying event (e.g.- Parkinson's disease)
4. Major psychiatric disorder which could lead to cognitive deficits
5. Severe aphasia
6. Severe hearing impairment
7. Those not speaking Tamil or English

An ischemic stroke is defined as ‘rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer, with no apparent cause other than of vascular origin’ in which a brain CT or MRI scan does not show intracranial haemorrhage.

An interval of 2-3 months following stroke onset for neuropsychological Testing is chosen to allow sufficient time for the acute stroke effects to subside.

Assessment Procedure:

The subjects were be subjected to structured medical and neurological history based on review of all available hospital charts, interview of the subject and a knowledgeable informant, and a structured clinical, neurological, neuropsychological, and neuroradiological evaluation. Patients will be retested at 3, 6, and 12 months after stroke. At the time of entry, the following data will be collected : (1) sex; (2) age (categorized as between 40 and 59, between 60 and 69, and ≥ 70); (3) education; (4) cerebrovascular risk factors, including cigarette smoking , hypertension (treatment or two or more measurements before stroke of systolic pressure 140 or diastolic pressure 90 mm Hg), diabetes (treatment or fasting blood glucose >7.8 mmol/L before stroke), hypercholesterolemia (total cholesterol >6.2 mmol/L), ischemic heart disease (previous myocardial infarction or angina), previous history of

transient ischemic attack or stroke, and atrial fibrillation; and (5) presence of aphasia in the acute phase of stroke.

In depth probes in the history for risk factors and features suggesting of pre-morbid cognitive impairment were attempted. Significant past medical history if any were noted. A thorough clinical examination was performed at the time of first visit. A routine screening, which included blood sugar, urea, serum creatinine, lipid profile, four-vessel doppler study, electrocardiogram, and echocardiogram were done at the time of admission.

In addition, to assess physical and non-physical functional abilities, the Blessed functional activity scale (BFAS), and the Barthel index (BI) were administered.

Neuropsychological Assessment:

The study population consisted of people speaking either the Tamil or English. Patients were of different literacy levels. The Vascular Dementia Battery was offered to all patients included in this study. The Vascular Dementia Battery assesses six cognitive domains: attention, language, verbal memory, visual memory, visuoconstruction, visuomotor speed and executive functions. The Mini-Mental State Examination (MMSE) was also administered together with the Vascular Dementia Battery .

Domains	Neuropsychological tests
Attention	Digit Span Forward
Language	Modified Boston Naming Test Verbal Fluency Test (Category naming of animals in 1 minute)
Memory	RAVLT
Visuoconstruction	Clock Drawing Test Crossing-pentagons item from MMSE
Visuomotor Speed	Digit Cancellation Task
Executive function	Trail-making test B

Of the 50 words used in RAVLT((Rey auditory verbal learning test), 42 were translated, back translated from the original list, and assessed for conceptual equivalence. Eight words were replaced by culturally appropriate words in the local language; for example, “turkey” was replaced by “peacock,” “ranger” was replaced by “policeman,” and “stocking” was replaced by “sock.”

The patients’ performance was compared with that of a group of normal control subjects from previous studies.

Neuroradiological assessment:

All patients underwent cranial imaging, either computed tomography (CT) scan or magnetic resonance imaging (MRI). MRI was done in 61 of 100 patients, and all 100 patients underwent CT scan.

Infarcts were identified on neuroimaging and classified as cortical, subcortical, or borderzone. Cortical infarcts were defined as infarcts of predominantly cortical location. Subcortical infarcts were further classified as lacunar and nonlacunar infarcts. Lacunar infarcts were defined as lesions 3-15 mm in diameter, located in the deep white matter or the basal ganglia. Subcortical infarcts >15 mm in size were classified as nonlacunar. Border-zone infarcts were located in the vascular border zone between the anterior cerebral artery (ACA), middle cerebral artery (MCA), or posterior cerebral artery (PCA) or between the superficial and deep branches of the cerebral arteries. Stroke volume was calculated by using the formulae $0.5 \times A \times B \times C$. (A – Largest transverse diameter of the infarct, B – Largest perpendicular diameter of the infarct, C – Vertical diameter, determined by summing the thicknesses of the slices in which the lesion was visible)

Diagnosis:

For dementia (Vascular Dementia) diagnosis, a subject must have fulfilled NINDS-AIREN criteria (the National Institute for Neurological Disorders and Stroke-Association Internationale pour la Recherche et a'Enseignement en Neurosciences). For a diagnosis of Vascular Mild Cognitive Impairment, the subject must have definite impairment in one domain and the functional decline criterion for Vascular Dementia was

not met. Impairment in a cognitive domain was defined as definite impairment (> 5 th percentile) on at least one test.

Vascular territory was inferred from the neurological deficit profile and the topography of relevant infarction on brain imaging obtained during their hospital stay, if positive, using the guidelines provided by Damasio. Territories included internal carotid, anterior cerebral, middle cerebral, posterior cerebral and vertebrobasilar arteries.

Vascular Dementia Subtypes:

Vascular Dementia was classified based on brain imaging as cortical Vascular Dementia in patients with multiple cortical infarcts, as subcortical vascular dementia when Vascular Dementia was associated with subcortical infarcts and/or white matter hyperintensities, or as cortical-subcortical Vascular Dementia in those with a combination of cortical infarcts and discrete subcortical infarcts/ white matter hyperintensities. Strategic infarct dementia was diagnosed when dementia could be explained by a single, strategically placed infarct. Subcortical vascular dementia was further classified depending on the predominant lesion type as subcortical vascular dementia due to subcortical infarcts, white matter hyperintensities, or a combination of the two. All infarcts, both symptomatic and silent, were taken into consideration.

Follow Up:

After informed consent, patients were re-examined 3, 12, and 24 months after stroke. In these visits, physical and neurological examinations, functional assessment, neuropsychologic battery, and diagnosis of Dementia and Vascular Mild Cognitive Impairment were performed.

RESULTS

Prevalence of Impairment:

Sixty percent of stroke patients were diagnosed as Vascular Cognitive Impairment. Twenty-three subjects were diagnosed as Vascular Dementia. Two subjects in the age range 40–59 years was diagnosed with Vascular Dementia, whereas 9 in the 60–69 years, and 12 in the ≥ 70 years group had this diagnosis. The prevalence of Vascular Mild Cognitive Impairment was 37% and forty percent of the patients had no cognitive impairment. (Table.1 and 2 , Figure.1 and 2)

Table. 1. Prevalence of Vascular Cognitive Impairment

No cognitive Impairment	40
Vascular Mild Cognitive Impairment	37
Vascular Dementia	23

Table .2. Prevalence of Impairment in various age groups

	40-59	60-69	≥70	Total
VaMCI	6	26	5	37
VaD	2	9	12	23
NCI	28	8	4	40

Subject Characteristics:

Of the 176 patients with ischemic stroke screened for study suitability, 119 met inclusion and exclusion criteria and were entered into the study. The major reasons for exclusion, in order of frequency, were presented in Table.3. and Figure.3.

By the time of detailed assessment at 3 months following the ischemic stroke, 8 were lost to follow-up (4 relocated outside Chennai and was not contactable, 3 died, 1 was refused for further follow-up). Of the 111 patients 100 completed follow-up at 1 year and 11 were lost to follow-up (2 died, 1 was reclassified as a patient with possible Alzheimer's disease, and 8 were not contactable).

Table.3. Major reasons for exclusion from study.

Serial No.	Reasons for exclusion	Number of persons excluded
1.	Refusal by subject or family member	17
2.	Critical medical condition	12
3.	Severe aphasia	9
4.	Pre-existing dementia clinically	5
5.	Those not speaking Tamil or English	5
6.	Neurological disorders other than qualifying event (e.g.- Parkinson's disease)	4
7.	No baseline CT	3
8.	Severe hearing impairment	2

The demographic and functional characteristics of the study sample were presented in Table.4. Mean age was 66.3 years (range 48 to 85). 29% of female patients were included in this study. Among the females fifty five percent had cognitive impairment whereas sixty one percent of male patients had the diagnosis of cognitive impairment.

Table .4. The demographic and functional characteristics

	All patients (n=100)	NCI (n=40)	VaMCI (n=37)	VaD (n=23)
Age, years	66.3	61.5	67.7	72.3
Female/Male	29/71	13/27	8/29	8/15
Education, years	8.6	9.9	8.2	6.9
MMSE	27.9	29.1	28.0	25.8
Barthel Index	85	90	85	65

Clinical Features:

Stroke subjects had a mean age of 66.3 years and 71% were men. The numbers in the age bands 40–59, 60–69, and ≥ 70 years were 36, 43, and 21, respectively. The putative cerebrovascular risk factors were presented in table 5 and figure 4. When the CT scans were carefully analysed, 68 of patients had brain infarcts, which were large infarcts in 24 patients. (Table.6 and Figure.5)

Table .5.Risk Factors.

Risk factors	Stroke patients	NCI	VaMCI	VaD
Hypertension	56	23	19	14
Hyper Cholesterolemia	34	13	15	6
Smoker	51	25	18	8
Diabetes mellitus	14	5	5	4
Previous TIA	18	5	8	5
Previous stroke	12	4	5	3
Previous AMI	17	6	7	4
Previous angina	19	6	6	7
Atrial fibrillation	11	4	3	4
Mean CVRF score	2.5	2.2	2.6	2.8

Table .6. Clinical and CT brain characteristics of the sample

	NCI (n=40)	VaMCI (n=37)	VaD (n=23)
Clinical stroke			
Laterality (right sided)	18	19	11
Lacunar infarct	13	9	5
Prior CVA	4	5	3
CT Brain Infarct Volume, mm ³	1430	860	4300

Comparison of Impaired with Non-Impaired Subjects:

Impaired subjects, those with Vascular Dementia or Vascular Mild Cognitive Impairment, were older but there were no sex differences in the two groups. They had 1.5 years less education than the non-impaired subjects. The two groups did not differ significantly on any particular cerebrovascular risk factor except that impaired patients had a higher overall number of risk factors in comparison to non-impaired patients. The two groups did not differ significantly on the side of stroke, whether the strokes involved the cerebral hemisphere or brain stem/cerebellum, and large or lacunar strokes. Vascular Dementia subjects had a slightly but significantly lower score on Barthel Index, indicating greater disability.

Comparison of Vascular Mild Cognitive Impairment with Vascular Dementia:

The Vascular Mild Cognitive Impairment group did not differ significantly from Vascular Dementia on age, sex, and education but, as expected, the Vascular Mild Cognitive Impairment had higher scores on the Mini Mental Status Examination, Barthel Index, and Blessed functional activity scale. Cerebrovascular risk factors and their numbers were similar in the two groups.

Subtypes of Vascular Dementia:

Twenty three subjects were diagnosed to have Vascular Dementia according to NINDS-AIREN criteria. Among these 43% had subcortical dementia , the commonest type of vascular dementia found in this study. Another 26% percent had cortical-subcortical type of dementia the second commonest type. Two patients had vascular dementia due to strategic infarct one due to bilateral thalamic infarct and another due to anterior opercular syndrome. (Table.7 and Figure.6)

Table.7. Subtypes of Vascular Dementia

Subcortical	10 (43%)
Cortical	5 (22%)
Cortical – Subcortical	6 (26%)
Strategic infarct	2 (9%)

Cognitive impairment and Vascular territory (Figure.7):

When cognitive impairment was examined by specific vascular territory and laterality (table 8), differences were less obvious, in part because of small samples in some of the subgroups. Overall, cognitive impairment appeared most frequently with infarcts in the left anterior and posterior cerebral artery territories and least frequently with infarcts in the

vertebrobasilar artery territory. Examining vascular distribution independently of hemispheric side, the proportion of infarcts in the anterior cerebral artery territory was higher among those with cognitive impairment (7.6%) compared with those without (3.4%) . Comparing left-sided, right-sided and vertebrobasilar strokes, left-sided damage was more common among those with cognitive impairment (n=28) compared with those without (n=17).

Table. 8. Cognitive impairment and Stroke territory

Stroke territory	Cognitive impairment	
	Present(n=60)	Absent(n=40)
Left ICA	1	0
Right ICA	0	1
Left ACA	3	2
Right ACA	2	2
Left MCA	19	13
Right MCA	18	10
Left PCA	6	4
Right PCA	5	2
Vertebrobasilar	6	6

Frequency Of Impairment in Neuropsychological Tests:

Comparing raw neuropsychological scores, patients with cognitive impairment were impaired on all 7 scored items of the neuropsychological battery (Table. 9). A higher score on memory, attention, visuospatial functioning, language, and MMSE denotes a better performance. A lower score on executive functioning or visuomotor tests corresponds with a worse performance, as these are speed measures. On average, patients with cognitive impairment performed worse than those without such damage. I found that age influenced cognitive performance on all domains (older age was negatively associated with cognitive performance). There were no differences between patients with cognitive impairment and patients without cognitive impairment in terms of depressive symptoms, both at 3 months and 12 months after stroke.

Baseline and 1-year follow-up classification of the 100 patients:

The baseline (3 months) and 12-months results of various clinical parameters are given in Table.10.

Table. 9. Frequency Of Impairment in Neuropsychological Tests

Neuropsychological Tests		NCI	VaMCI	VaD
Digit span forward		6.1	5.0	4.2
Modified Boston Naming Test		13.8	10.2	7.1
Category naming of animals in 1 minute		17.0	13.7	10.8
RAVLT	Delayed recall	10.1	9.0	6.2
	Recognition	13.6	11.5	9.1
Clock Drawing Test		4.7	3.8	3.2
Trail-making test B		123	191	262

Table . 10. Baseline and Follow-up results of clinical parameters

Tests	NCI		VaMCI		VaD	
	At 3 months	At 12 months	At 3 months	At 12 months	At 3 months	At 12 months
MMSE	29.1	29	28.0	28.6	25.8	22.2
Barthel Index	89.9	92.4	79.1	79.9	68.7	71.5
BDI	9.7	9.6	13.6	13.8	15.9	15.8
Digit span forward	6.1	6.6	5.0	6.1	4.2	4.9
Trail-making Test B	123	98	191	170	262	201
Modified Boston Naming Test	13.8	14.1	10.2	10.7	7.1	9.1

Of the 100 stroke patients who were reassessed, the baseline and 1-year follow-up classification are tabulated in Table. Eighty patients had the same classification as at baseline. Of the 20 patients who had a changed classification, the majority were ‘Vascular Mild Cognitive Impairment’ at baseline with 10 improving to ‘No Cognitive Impairment’ and three deteriorating to ‘Vascular Dementia’—an annual conversion rate (from ‘Vascular Mild Cognitive Impairment’ to ‘Vascular Dementia’) of 8%. The annual rate of deterioration from ‘No Cognitive Impairment’ to ‘Vascular Mild Cognitive Impairment’ was 10% but none of this group of patients became ‘demented’. (Table .11)

Table .11. Baseline and Follow-up classification of Cognitive impairment.

		Classification at 1-year follow-up			
		NCI	VaMCI	VaD	Total
Classification at baseline	NCI	36	4	0	40
	VaMCI	10	24	3	37
	VaD	0	3	20	23

Relationship to functional status:

Severity of functional impairment was significantly greater with cognitive impairment, measured by the Barthel Index, Blessed functional activity scale and NIH stroke severity scale. Moreover, dependent living after discharge, either at home or nursing home, was more likely (46% with, 27% without cognitive impairment). (Table . 12)

Table .12. Cognitive impairment and Functional Status

		Cognitive impairment	
		Present (n=60)	Absent (n=40)
Functional and physical impairment	Barthel, mean (SD)	77.0 (27.9)	89.9 (17.8)
	BFAS, mean (SD)	3.8 (3.9)	1.5 (2.0)
Status after discharge	Independent	32	29
	Dependent	28	11

DISCUSSION

The Prevalence Rate:

The prevalence rate of Vascular Dementia is 23% in a well characterised cohort of stroke subjects examined 3 months after the index event. All cases of Vascular Dementia, bar two, were diagnosed in those over 60 years. The figures are consistent with previous reports, with one previous study [39, 40] reporting a rate of 26.4% in individuals aged 60–90 years, and another study [41] reporting a rate of 25% in individuals 55–85 years old.

Epidemiologic studies from India have shown that Vascular Dementia is a common form of dementia, in contrast to the West. This finding may be related to the overall reduced life span in Indians and the increasing burden of cardiovascular disease, including stroke. Recent observations of the decreased prevalence of Vascular Dementia in Japan, attributed to decreased incidence of stroke and westernization, support this hypothesis.

Relationship between age and prevalence:

Age was a significant determinant of prevalence in this study only when more than 60 years was used as the cut-off, i.e. the prevalence rate did not increase after the age of 60 years. In the New York study, subjects

in their 60s had a lower rate than those 70 years and older. When age was entered into logistic regression along with other possible determinants of dementia, it was no longer significant. This is possibly because age is correlated with cerebrovascular risk factors as well as brain imaging parameters such as atrophy and White matter hyperintensities. It can be concluded that a stroke in an older person is more likely to produce dementia than in someone less than 60 years. This is considered to be due to the additional cerebrovascular pathology in older brains, which may be due to previous infarctions and non-infarct ischemic changes. The role of Alzheimer-type pathology in older brains is another important factor, with post mortem examination necessary to determine its relative contribution.

Vascular Dementia Prevalence:

The prevalence rate of Vascular Dementia in this study compares well with other hospital-based populations [39, 40, 41] even though the definition of dementia used in this study was different, an issue discussed below. The rates of the hospital-based studies are much higher than the rate reported from the Framingham Study in which subjects who had been examined prior to the stroke were followed up for 10 years after the stroke [42] . The rate of dementia was 19.3% in stroke patients compared to 11.0% in controls, suggesting a twofold increase in risk of stroke over a 10- year period in the community-based sample [42] . This compares

with a nine fold increase reported in a cross-sectional study immediately following stroke [40] . It is possible that strokes in the community sample were less severe.

The NINDS-AIREN [43] criteria used in this study may also have played a role as they are insensitive to subcortical dementia. The reason that I chose these criteria was to minimize the inclusion of patients with Alzheimer's disease or mixed dementia in this VaD group. It is increasingly being recognized that vascular and Alzheimer's disease pathologies frequently coexist in dementia. To exclude such patients with mixed dementia from a clinical study is challenging. Clinicopathologic studies have demonstrated that NINDS-AIREN criteria for VaD have high specificity for pure VaD. Therefore, within VaD group, the possibility of patients with coexisting Alzheimer's pathology is reasonably low. Third, different criteria for diagnosing VaD may explain differences between series. However, NINDSAIREN criteria are the most widely used criteria for VaD.

In this study, subcortical dementia due to multiple lacunar infarcts and/or WMHs was the most common subtype of VaD, whereas dementia due to multiple cortical infarcts and single strategic infarcts was less common. Similar patterns of VaD have been reported in Japanese and Western populations.

Impact from pre-existing dementia:

The subjects in the Framingham Study were selected for their lack of dementia at baseline, which was made possible by the longitudinal design. In this cross-sectional study, I attempted to do this by retrospective assessment using the IQCODE (The Informant Questionnaire on Cognitive Decline in the Elderly), an informant based assessment of cognitive decline prior to the stroke. I excluded 5 subjects primarily on this criterion. In spite of this exclusion, IQCODE score remained a weak predictor of dementia diagnosis, and it is likely that in other studies that did not have such exclusion, the contribution of pre-existing pathology was greater. Previous studies have shown that pre-existing cognitive deficits are common in this sample [41, 44], and post-stroke dementia should not be considered to be new onset dementia.

Criteria for Vascular Dementia:

The definition of Vascular Dementia used is an important consideration in the interpretation of prevalence rates. The construct of Vascular Dementia is still evolving and the currently available criteria sets have low correspondence with each other [45, 46]. The criteria used in this study differed from those used in other studies in that memory

impairment was necessary for the diagnosis of Vascular Dementia. This is similar to the DSM-IV criteria [47] but different from the ADDTC [43]. Unlike the ADDTC criteria, however, the presence of two or more ischemic strokes or one or infarcts on CT or T 1 -weighted MRI was not necessary, and extensive white matter disease was sufficient for the diagnosis. Another feature of my diagnoses was that the neuropsychological and functional criteria were operationalised, and the significance of the vascular pathology was based on CT or MRI scans. CT scans were available for all patients. However, the decision whether the vascular pathology on brain scans was sufficient to account for the cognitive impairment was based on ‘clinical judgement’. The presence of an infarct was not considered necessary if the subject had extensive white matter pathology, although most subjects had a combination of the two kinds of lesions. Furthermore, memory impairment was not an essential criterion for the diagnosis of impairment or dementia. Applying the non-memory impairment criterion to our definition of dementia would have changed the prevalence considerably. Six of the VaMCI subjects had marginal or definite memory impairment in either verbal or non-verbal domain, and would have met the NINDSAIREN criteria.

Prevalence of VaMCI:

This study also reports the prevalence of MCI in this sample, presumably again of vascular origin. More than one third of stroke subjects met the criteria for MCI, and the combined Vascular Dementia and Vascular Mild Cognitive Impairment groups accounted for nearly 60% of the sample. This suggests that the majority of stroke subjects have cognitive impairment, with about a quarter reaching the threshold for dementia diagnosis. I was interested in knowing whether the determinants for dementia were qualitatively or quantitatively different from those for Vascular Mild Cognitive Impairment.

Stroke related factors:

Previous studies have identified some stroke-related factors as determinants of dementia, in particular lacunar infarcts, left-sided lesions and hemispheric infarcts [39, 49]. A major dominant stroke syndrome and dysphasia have also been related to dementia [49, 50]. These findings have, however, not been consistent, with other studies failing to support these relationships [51], including this study. Since this study necessitated a demanding assessment schedule, it is likely that many severely ill subjects were excluded. I also excluded subjects with severe aphasia or non-fluency in Tamil or English because of the difficulty in obtaining

informed consent and assessing neuropsychological function. This may have contributed to the lack of a left-hemispheric bias in this dementia subjects.

Risk factors and Cognitive impairment:

Hypertension, diabetes [51], atrial fibrillation [52, 53] and other recognised cerebrovascular risk factors have emerged as independent risk factors for dementia in some studies but not others. In the Framingham Study, after stroke had been accounted for, exposure to individual risk factors did not alter the hazard ratio. The analysis in this study did suggest that overall cerebrovascular risk factor exposure was associated with cognitive impairment, but it was not significant in the combined regression analysis.

Stroke Volume:

In the brain imaging parameters, this study assessed only total stroke volume. It was significant (OR 1.8). Brain atrophy in this study, being measured after the stroke, does not accurately reflect baseline atrophy since it is confounded by the stroke itself. I had hypothesised that stroke volume and number would be independent predictors of dementia, and this was only partially borne out. About 70% of our subjects had this event as the first clinical stroke, and the multiple infarcts seen in many

subjects were lacunar and small in volume. Such subjects were more likely to have extensive White matter hyperintensities. That I found White matter hyperintensities to be greater in those with cognitive impairment is consistent with some previous reports [49, 51] and the literature reporting a relationship between WMHs and cognitive impairment [54]. It also reflects the definition of Vascular Dementia used by others previously: the presence of an infarct was not necessary if extensive White matter hyperintensities were present on MRI, and deficits in any two cognitive domains were sufficient for the diagnosis without memory being specifically affected. MRI scans were not always available on this subject. In such cases, CT scans were used to assess white matter disease. The threshold for significant white matter lesions was therefore high and White matter hyperintensities on T2-weighted FLAIR imaging were considered clinically significant if abnormality was also seen on CT scans.

Depression:

Some other factors that were non-significant must be commented upon. Depression was not significantly different in the two groups. It is noteworthy that in those with depression, the neuropsychological assessment was postponed until remission had occurred.

Functional status and cognitive impairment:

The presence of cognitive impairment significantly correlated with dependent living after discharge from the hospital (whether requiring nursing home or home attendant care). Although this finding is neither novel nor unexpected, it emphasises the potential value of neuropsychological assessment of patients with stroke. Yet mental function tests have largely been ignored or limited in both observational outcome studies [55] and interventional clinical trials aimed at minimising neurological disability from ischemic stroke.[56]

Follow-up:

A more recent analysis of the Canadian Study of Health and Ageing cohort, showed that nearly half of those who had “vascular cognitive impairment without dementia” developed dementia within 5 years [57]. These findings are similar to previous estimates of the likelihood to progression to dementia in Mild Cognitive Impairment (MCI) individuals [58,59]. Moreover, those who are ‘cognitively impaired but not demented’ had a high risk of converting to dementia, comparable to the results from the Canadian Study of Health and Ageing cohort.

LIMITATIONS

This study had a number of limitations.

- ✓ Firstly, this is a cross-sectional study with subjects being assessed only after the stroke had occurred. In spite of the exclusion of subjects with baseline cognitive impairment prior to stroke, it cannot be certain that subjects with mild cognitive impairment on the basis of Alzheimer-type pathology did not enter the study.
- ✓ Secondly, a large proportion of subjects were excluded for various reasons, but I do not consider it to have introduced a systematic bias in this sample based on the analysis of the minimal data available on those excluded. However, the more severely affected patients were likely to be excluded. The prevalence rates were possibly underestimated by this study for this reason.
- ✓ Thirdly, not all subjects had an MRI scan, thereby reducing the power of detecting differences in neuroimaging parameters.
- ✓ Fourthly, genetics data were not available, and therefore the contribution of apolipoprotein E polymorphism to the diagnostic status could not be examined.
- ✓ I used NINDS-AIREN criteria, which are known to have low sensitivity.

CONCLUSION

1. This study supports the high prevalence of dementia and mild cognitive impairment following stroke, especially in older individuals, and highlights the importance of cognitive reserve.
2. The contribution of cerebrovascular risk factors is not independent of the stroke risk.
3. Subcortical dementia was the most frequent subtype of Vascular Dementia in our hospital-based series.
4. Stroke volume is a significant determinant of post-stroke dementia.
5. This study suggests that cognitive performance in stroke patients may change over time. It also suggests that progression of cognitive impairment is common after stroke.
6. The cognitive impairment is not only frequent with stroke, but also significantly affects functional adaptation after the acute phase. Efforts to modify the course of acute stroke should also take into account "chronic brain failure" as an outcome.

Figure. 1. Prevalence of Vascular Cognitive Impairment

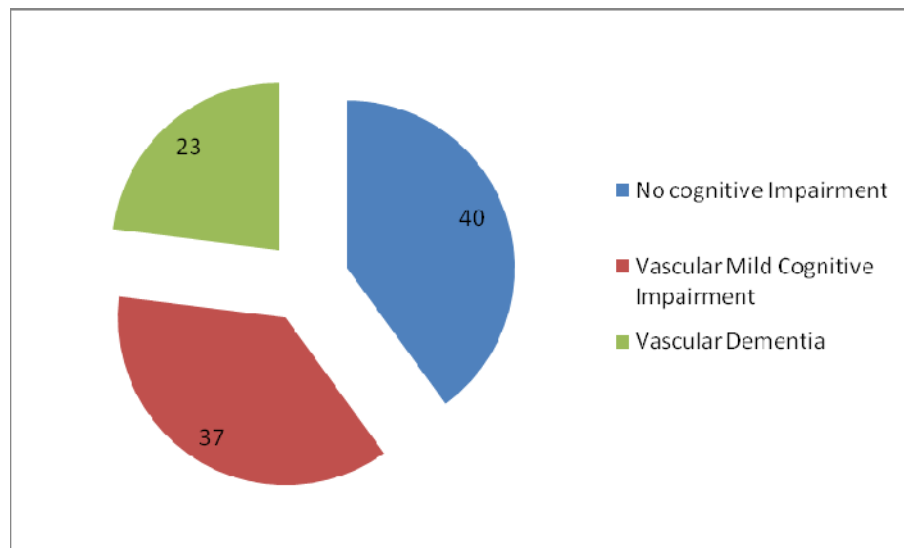


Figure. 2. Prevalence of Impairment in various age groups

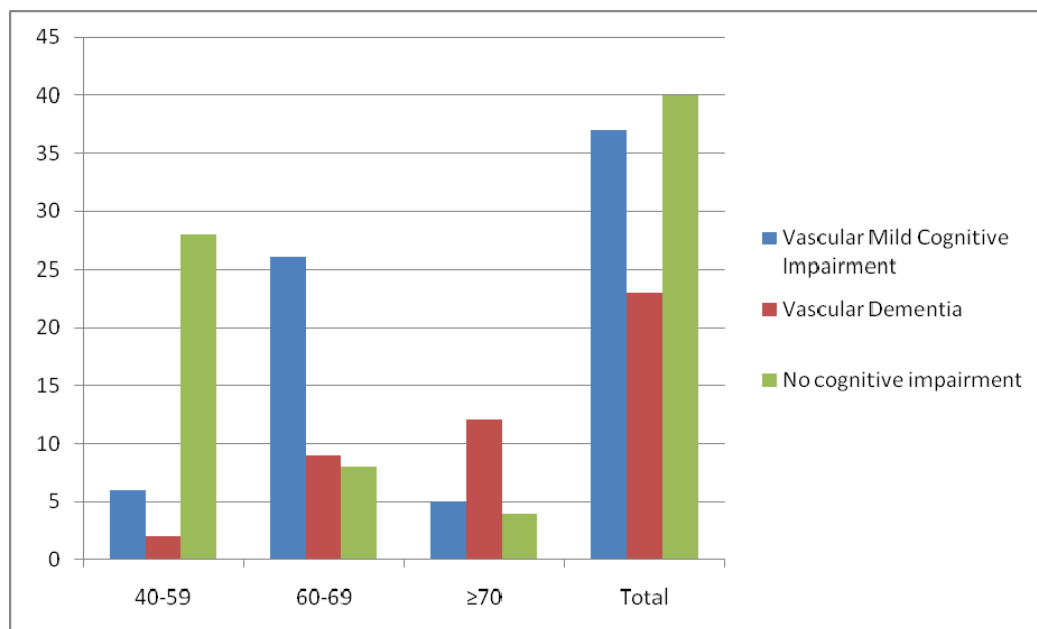


Figure .3. Reasons for exclusion from study

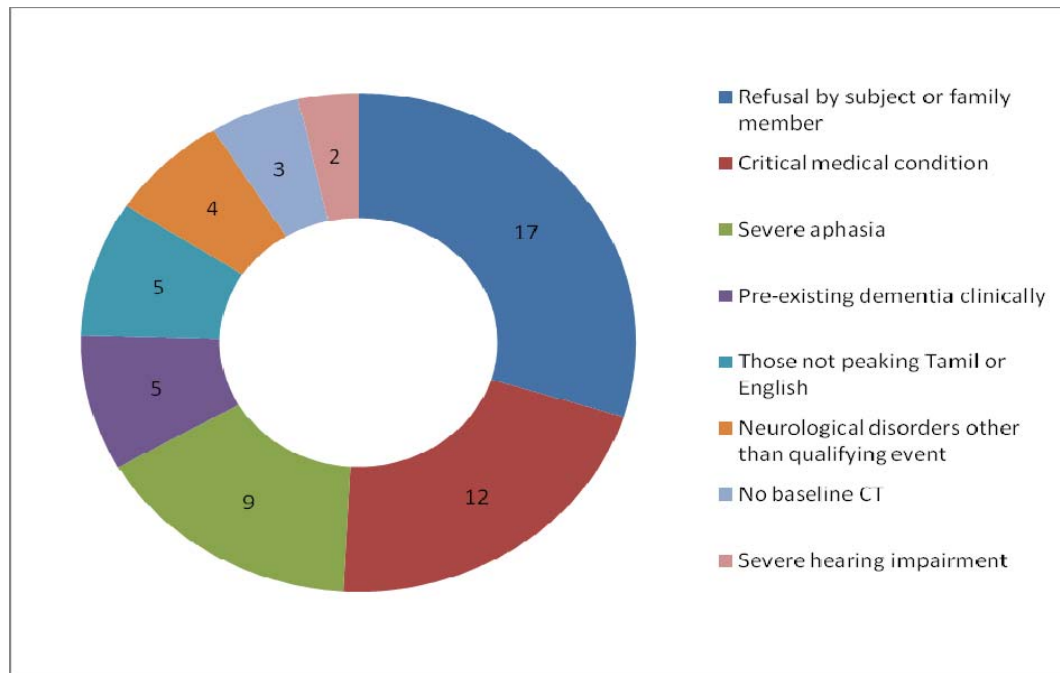


Figure. 4. Risk Factors

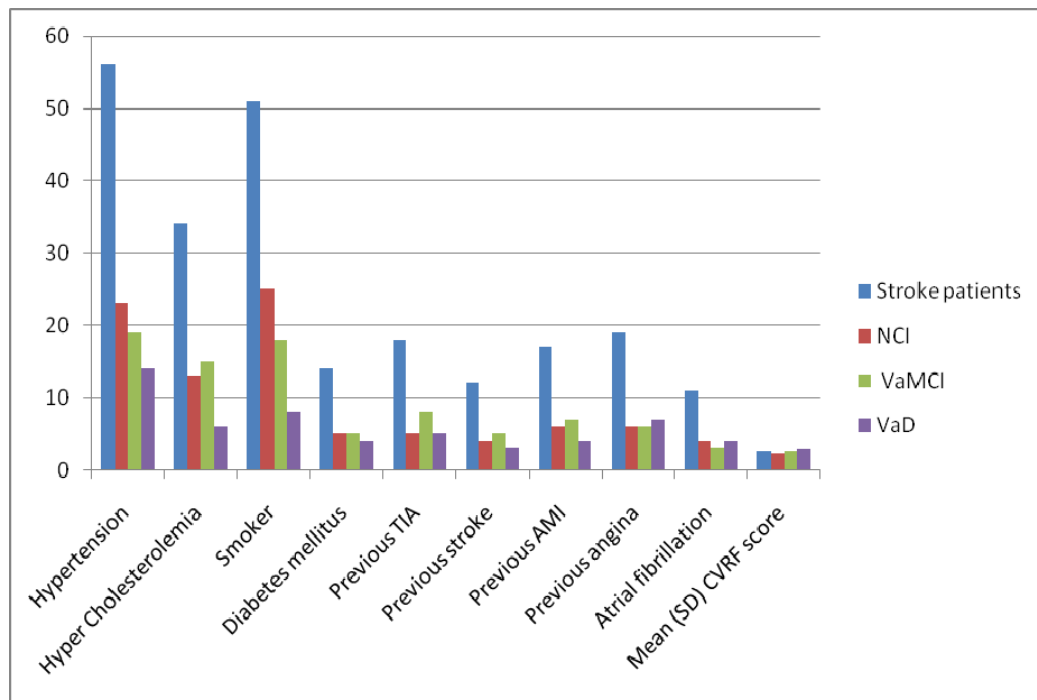


Figure.5. Stroke Volume

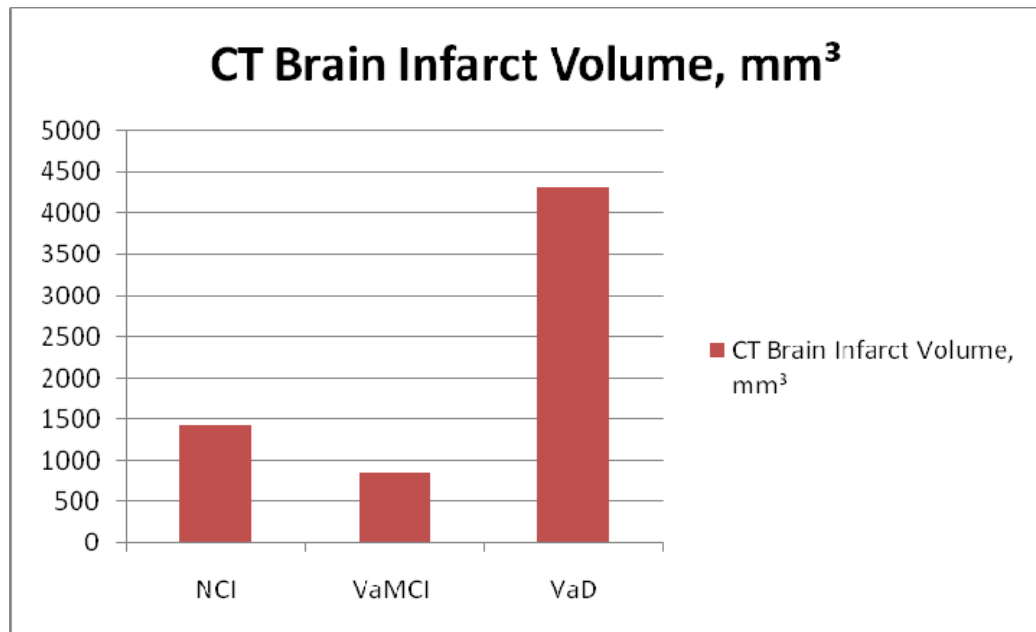


Figure. 6. Subtypes of Vascular Dementia

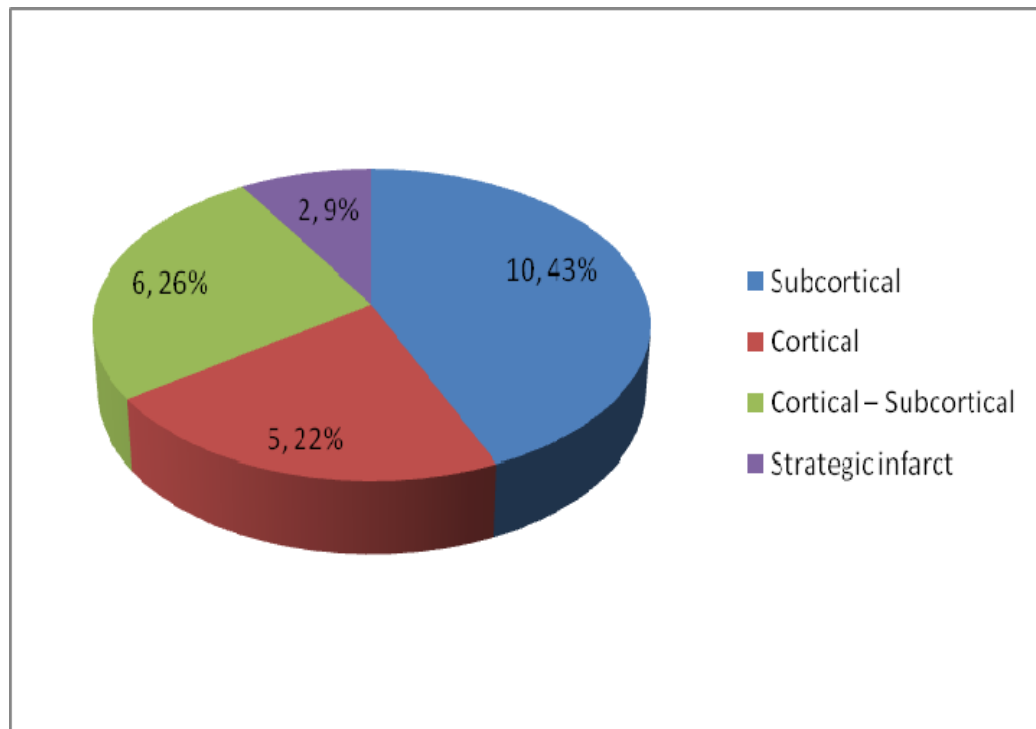


Figure. 7. Cognitive impairment and Vascular territory

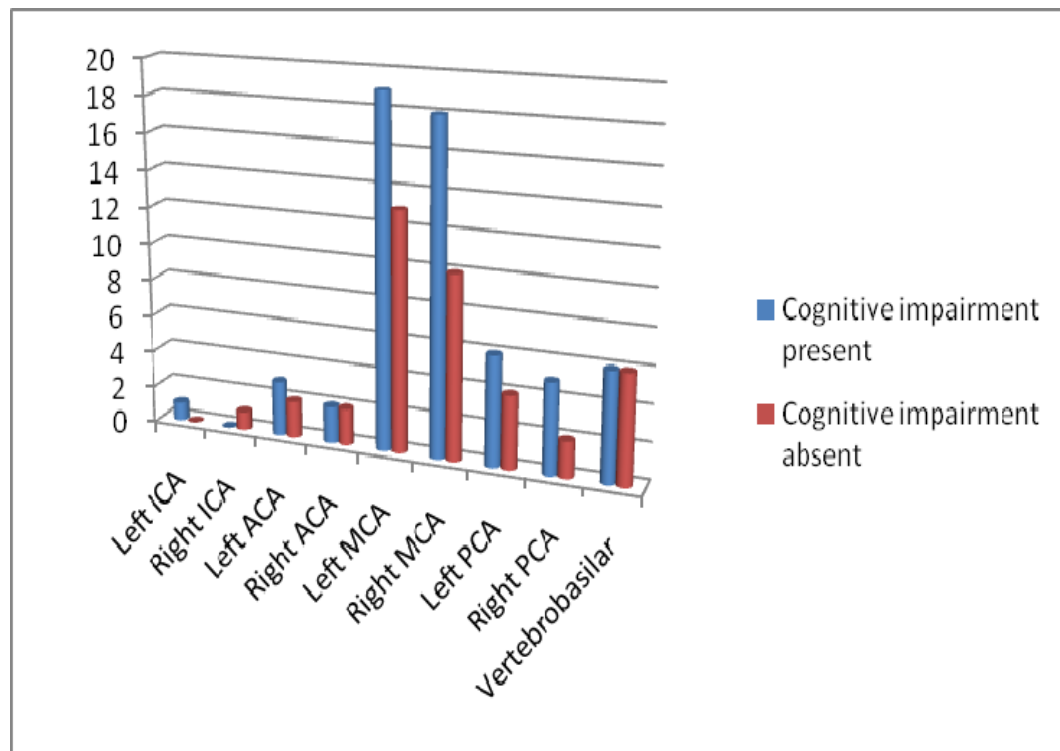


Figure. 8. Clock Drawing Test in a 59 years old VaMCI patient

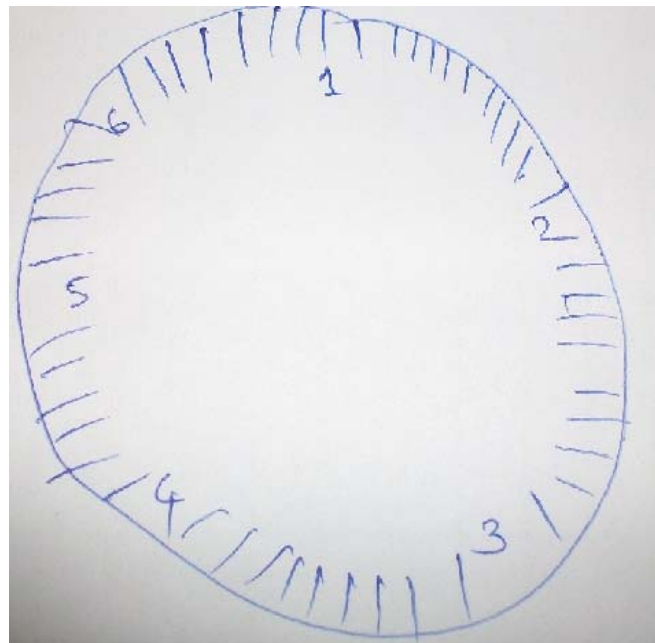


Figure. 9. Trail Making Test – B in a 66 years old VaD patient

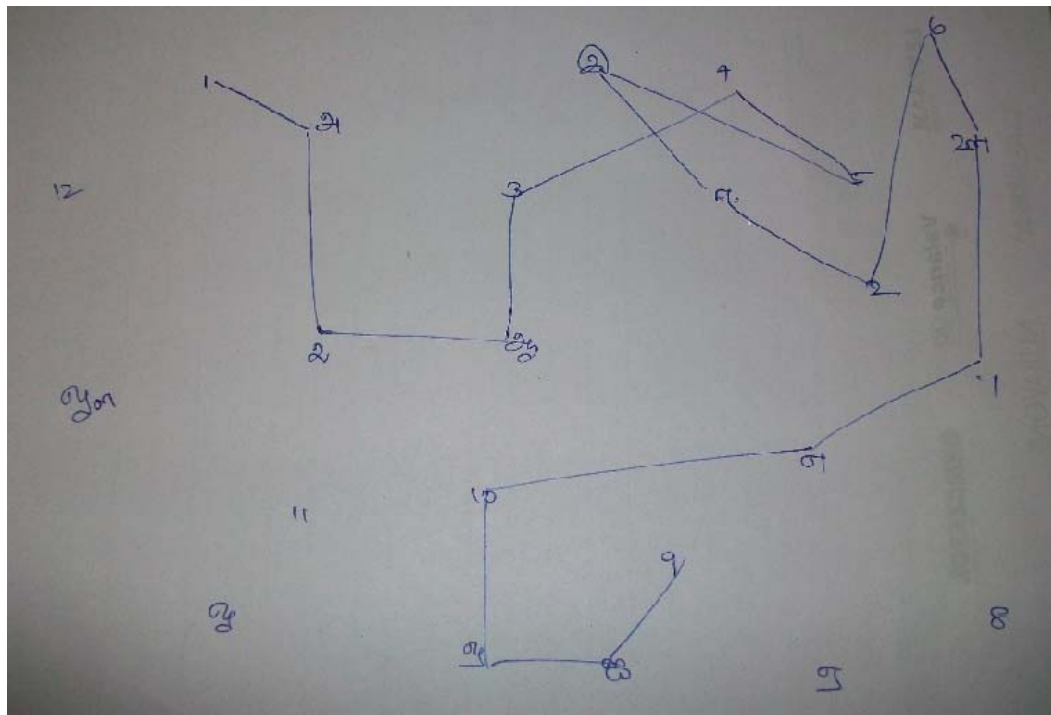


Figure.10. Digit cancellation test in a 68 years old male with NCI

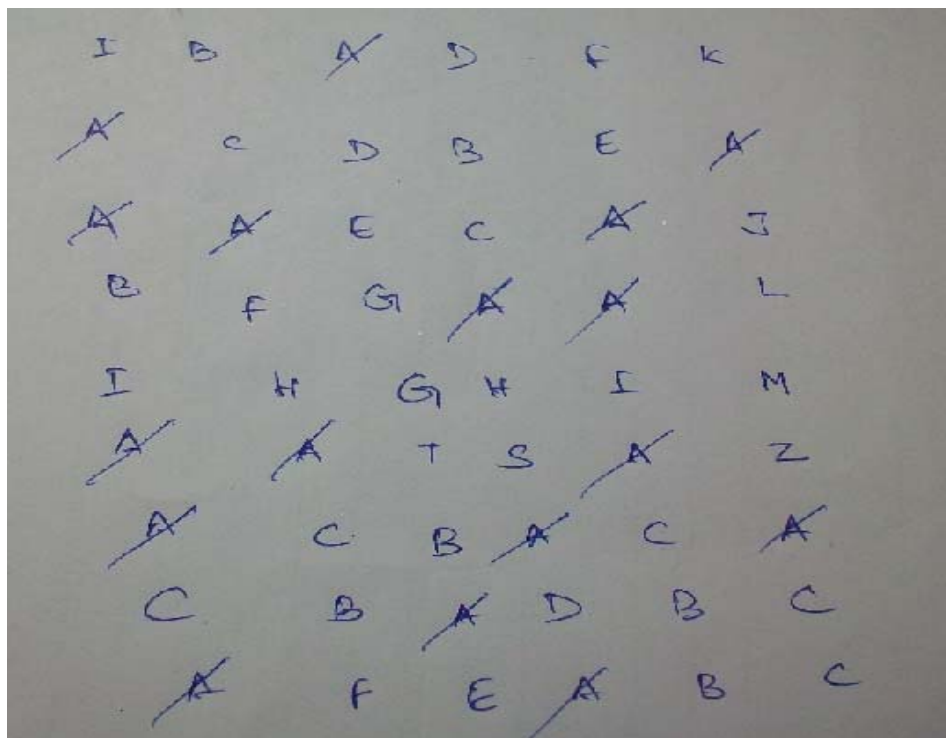


Figure. 11. Perseveration in a 71 yeras old VaD patient

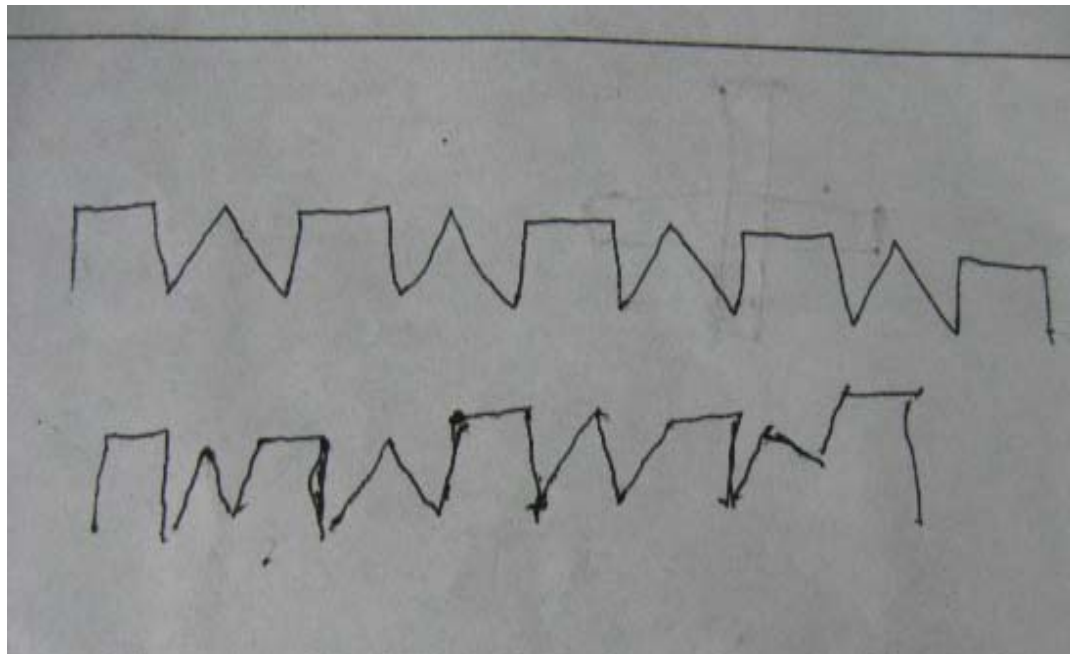


Figure . 12. A case of anterior opercular syndrome (Unilateral)

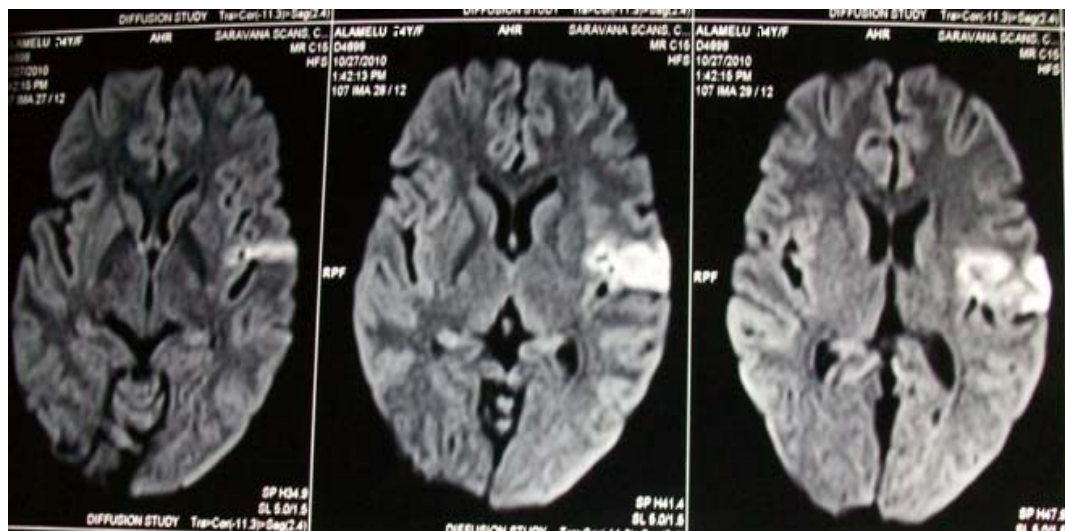


Figure . 13. A case of Acute stroke with Dense MCA sign on right side

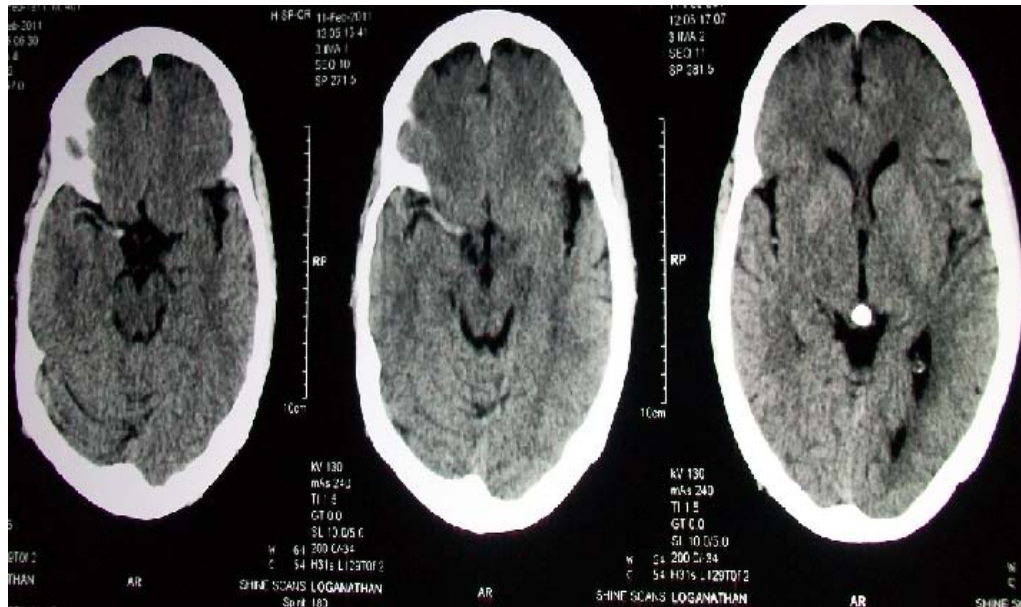


Figure . 14. Acute stroke-induced cytotoxic edema in the right cerebellar hemisphere(Diffusion- weighted MR image)

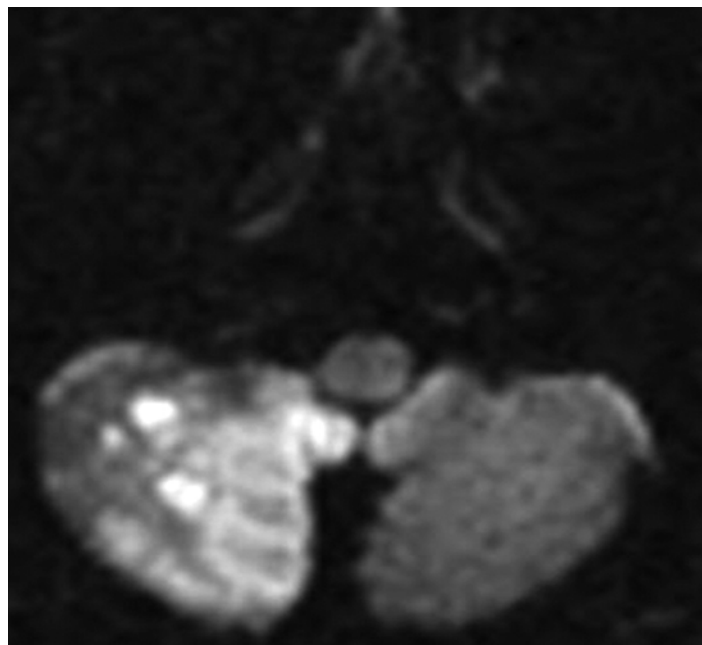
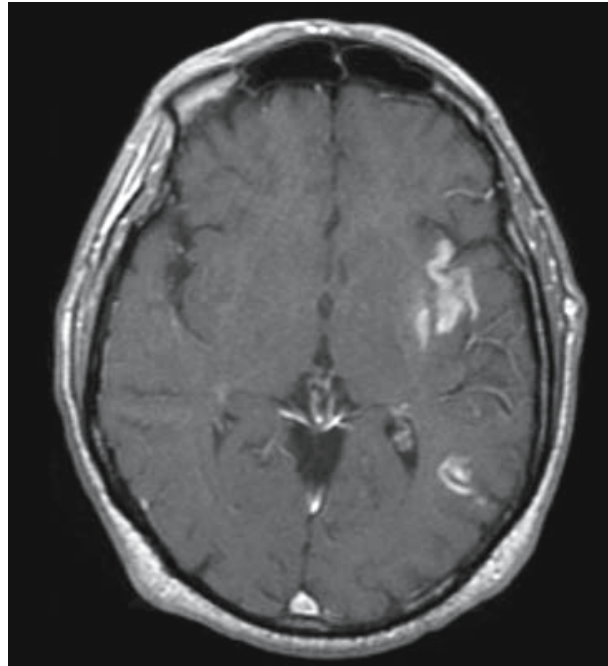


Figure . 15. Enhancing infarcts. Post contrast T1-weighted image shows gyriform enhancement at the left insula and posterior parietal lobe from a subacute left MCA infarct



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PATIENT CONSENT FORM

STUDY TITLE: Clinical Determinants and one year follow-up of Dementia and Mild Cognitive Impairment following Ischemic Stroke

Study Centre : Institute of Neurology, Madras Medical College & Govt.
General Hospital, Chennai – 03.

Patient's Name :

Patient's Age :

Identification Number: Patient may check () these boxes

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask the question and all my questions and doubts have been answered to my complete satisfaction.

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving any reason, without my legal rights being affected.

I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethics committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the study. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study.

I agree to take part in the above study and to comply with the instructions given during the study and to faithfully co-operate with the study team, and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms.

I hereby consent to participate in this study on "Clinical Determinants and one year follow-up of Dementia and Mild Cognitive Impairment following Ischemic Stroke"

I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical, radiological and urine examination.

Signature / Thumb Impression _____ Place _____ Date _____

Patient's Name and Address:

Signature of the Investigator: _____ Place _____ Date _____

Study Investigator's Name:

சுய ஒப்புதல் படிவம்
ஆய்வு செய்யப்படும் தலைப்பு

“மூளை இரத்தக் குழாய் அடைப்பால் ஏற்படும்
ஞாபக மறதி நோய் பற்றிய ஆய்வு”

ஆராய்ச்சி நிலையம் : நரம்பியல் பயிலகம்,
சென்னை மருத்துவக்கல்லூரி,
சென்னை - 600 003.

பங்கு பெறுபவரின் பெயர் :

பங்குபெறுபவரின் எண் :

பங்கு பெறுவர் இதனை (✓) குறிக்கவும்.

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டது.

☐

நான் இவ்வாய்வில் தன்னிச்சையாகதான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.

☐

இந்த ஆய்வு சம்மந்தமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன்.

☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையோ, முடிவையோ பயன்படுத்திக் கொள்ள மறுக்க மாட்டேன்.

☐

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன்.

☐

பங்கேற்பவரின் கையொப்பம் இடம் தேதி

பங்கேற்பவரின் பெயர் மற்றும் விலாசம்:

சாட்சியின் கையொப்பம்:

இடம் தேதி

சாட்சியாளரின் பெயர் மற்றும் விலாசம்:

ஆய்வாளரின் கையொப்பம்:

இடம் தேதி

ஆய்வாளரின் பெயர்

PROFORMA

Clinical Determinants and one year follow-up of Dementia and Mild Cognitive Impairment following Ischemic Stroke

Name: Place:
Age/sex: Handedness:
MIN No: Education:
Occupation: Contact No:

Complaints:

Risk Factors and Premorbid State:

Examination Findings:

Neuropsychological Assessment:

A. MMSE:

B. Vascular Dementia Battery:

Domains	Neuropsychological tests	Score
Attention	Digit Span Forward	
Language	Modified Boston Naming Test Verbal Fluency Test (Category naming of animals in 1 minute)	
Memory	RAVLT	
Visuoconstruction	Clock Drawing Test Crossing-pentagons item from MMSE	
Visuomotor Speed	Digit Cancellation Task	
Executive function	Trail-making test B	

Other defects in Higher Cognitive Functions:

Investigations:

1. CT findings
 - a. Site of acute lesion
 - b. Volume of the acute lesion
 - c. Old asymptomatic lesions
 - d. Total volume of all lesions, recent and old
 - e. Leukoaraiosis
 - f. Presence of cortical and subcortical atrophy
2. Blood Sugar- F- PP-
3. Sr.Cholesterol
4. ECG
5. Echo
6. 4-Vessel Doppler
7. Others:

Follow Up:

S.No	Name	Age	Sex	Education	Risk factors	Lateralisation	MMSE	Digit span	BNT	CNA	RAVLT - D	RAVLT - R	CDT	TMT	Territory	Diagnosi s
1.	Anbarasi	63	F	7	3478	R	25	5	5	8	6	9	1	261	7	VaD
2.	Amsam	49	F	10	243	R	30	5	9	13	8	12	5	135	6	NCI
3.	Ravi	6	M	10	23	L	30		9	13	8	12	5	233	5	VaMCI
4.	Kumari	57	F	12	19	R	29	7	10	12	10	11	5	150	2	NCI
5.	Kannan	66	M	9	57	L	29	7	8	14	7	14	4	154	6	VaMCI
6.	Manohar	63	M	6	236	L	30	6	10	12	9	13	5	170	5	NCI
7.	Kannan	48	M	10	34	L	21	3	8	10	10	14	5	293	8	VaD
8.	Gopi	54	M	5	12	L	26	5	12	9	11	13	4	190	3	NCI
9.	Mari	66	M	12	128	R	23	4	12	11	10	11	3	164	6	VaMCI
10.	Kuppan	71	M	12	35	R	22	6	13	14	7	12	4	279	1	VaD
11.	Mangai	65	F	D	47	R	19	5	5	13	5	9	3	187	3	VaD
12.	Satasivam	67	M	7	13	R	30	6	10	12	12	13	5	90	5	NCI
13.	Kiruki	63	F	8	156	L	30	5	9	9	8	11	5	80	6	NCI
14.	Munian	68	M	D	136	R	19	3	10	14	8	10	4	175	4	VaMCI
15.	Vijayan	61	M	5	238	L	30	8	7	9	7	11	5	178	5	VaMCI
16.	Venkat	75	F	5	12	L	29	7	8	11	8	10	3	100	5	VaMCI
17.	Vinayagan	59	M	7	13	R	30	4	9	9	7	12	4	100	5	NCI
18.	Vadivel	72	M	D	123	L	30	6	10	11	8	12	5	90	6	NCI
19.	Nithya	52	F	12	129	R	29	5	11	9	12	13	5	120	6	NCI
20.	Mani	61	M	5	89	L	23	4	7	5	3	5	3	376	9	VaD
21.	Veerasamy	63	M	0	28	R	23	6	12	13	7	9	2	311	5	VaMCI
22.	Varathu	74	M	3	3	R	25	3	3	5	2	6	4	190	7	VaD
23.	Mohan	54	M	5	24	R	28	5	11	9	8	13	5	100	5	NCI
24.	Vanaja	61	F	7	256	L	30	7	10	10	8	12	5	110	6	NCI
25.	Chellappan	60	M	9	125	L	22	3	9	9	6	9	2	125	6	VaMCI
26.	Maruthai	60	M	3	28	R	30		7	10	8	12	5	120	6	VaMCI
27.	Raja	68	M	2	9	R	27	3	10	9	5	8	2	432	6	VaD
28.	Aran	62	M	D	27	L	29	3	11	9	7	13	4	240	6	VaMCI
29.	Maran	58	M	10	137	R	29	5	10	9	10	11	5	100	7	NCI
30.	Ammavasai	63	M	8	123	L	30	7	8	8	9	10	3	99	7	VaMCI
31.	Mannar	76	M	11	45	L	21	3	6	12	7	11	5	403	6	VaD
32.	Meena	52	F	9	128	R	9	4	8	9	9	9	4	158	4	NCI
33.	Veerasami	49	M	11	12	L	30	5	11	12	6	19	5	95	5	VaMCI
34.	Mannar	63	M	10	245	R	30	6	9	11	11	14	4	176	3	VaMCI
35.	Mahamayi	71	F	8	13	L	30	5	10	11	12	12	4	160	3	NCI
36.	Namashi	71	M	12	2	L	30	4	7	12	10	14	4	156	7	VaMCI
37.	Nalini	68	F	9	157	R	29	5	9	10	8	12	5	140	5	NCI
38.	Alamelu	73	F	D	1258	L	19	5	5	11	4	9	5	188	5	VaD
39.	Devi	62	F	0	13	R	29	5	14	10	6	9	5	200	5	VaMCI

S.No	Name	Age	Sex	Education	Risk factors	Lateralisation	MMSE	Digit span	BNT	CNA	RAVLT - D	RAVLT - R	CDT	TMT	Territory	Diagnosi s
40.	Appusamy	65	M	5		L	26	5	12	12	7	11	3	180	5	VaMCI
41.	Malaya	57	M	8	23	L	27	7	6	9	9	12	4	211	5	VaMCI
42.	Latha	49	F	D	149	L	30	7	13	17	10	14	5	130	6	NCI
43.	Lakshmi	65	F	12	23	R	30	6	13	13	12	14	5	125	7	NCI
44.	Sanmugam	77	M	3	14	L	30	6	10	12	12	13	5	120	7	NCI
45.	Rajesh	71	M	5	48	R	29	4	8	11	5	6	3	284	8	VaD
46.	Rani	67	F	4	136	R	28	7	8	9	10	12	4	124	5	VaMCI
47.	Muniammal	68	F	2	257	R	30	5	11	13	8	12	4	150	5	VaMCI
48.	Lakshmi	49	F	0	156	R	30	5	10	10	12	11	5	160	4	NCI
49.	Tamilvanan	77	M	6	13	L	28	5	9	13	6	7	3	251	8	VaD
50.	Veeratha	59	F	7	168	L	29	5	10	11	7	12	5	168	6	NCI
51.	Mariyayi	61	F	12	125	L	23	3	10	11	4	8	5	134	9	VaMCI
52.	Vinayan	61	M	5	13	L	25	7	12	13	12	12	4	190	6	NCI
53.	Kittu	73	M	4	24	R	30	6	6	14	5	9	3	129	6	VaMCI
54.	Kavitha	50	F	4	269	R	30	4	10	10	10	11	4	110	5	NCI
55.	Kuppathal	62	F	2	26	L	27	3	7	10	3	8	1	201	5	VaD
56.	Sathya	67	F	3	57	L	22	2	4	9	5	5	4	187	9	VaD
57.	Chellappan	52	M	7	23	R	30	5	7	11	6	9	2	165	5	VaMCI
58.	Raniamma	56	F	D	2	R	29	6	11	12	10	13	5	115	7	NCI
59.	Dhanam	55	M	7	23	L	29	5	10	11	11	13	4	170	6	NCI
60.	Amuthan	65	M	5	13	R	29	5	8	9	11	13	4	208	7	VaMCI
61.	Malar	52	F	6		L	30	5	9	9	8	9	5	175	5	NCI
62.	Dhandabani	57	M	4	25	R	29	7	12	13	12	14	5	180	6	NCI
63.	Rajam	55	F	9	15	L	30	6	11	12	13	12	5	180	5	NCI
64.	Pandian	70	M	8	127	R	21	3	8	12	4	7	5	302	5	VaD
65.	Pavadaiammal	67	F	7	124	L	30	5	8	11	10	12	5	177	7	VaMCI
66.	Ramesh	55	M	12		L	30	5	9	12	11	12	5	140	5	NCI
67.	Narayanan	72	M	3	18	L	23	6	6	11	6	8	2	295	5	VaD
68.	Murugaye	57	F	10		L	30	6	10	10	12	12	4	120	6	NCI
69.	Rajavel	70	M	5	13	R	24	5	9	13	10	13	3	243	7	VaD
70.	Mannar	58	M	10	156	R	30	5	10	13	5	9	2	165	6	VaMCI
71.	Melakka	56	F	0	159	L	25	4	13	13	9	10	4	254	6	VaD
72.	Mallika	75	F	0	25	R	30	5	10	12	12	12	4	254	7	NCI
73.	Mayilan	78	M	1	2	R	30	5	7	8	8	12	4	100	9	VaMCI
74.	Chellayi	53	F	3		L	30	6	9	9	10	10	5	140	6	NCI
75.	Meera	51	F	7	27	L	30	7	12	13	13	13	5	85	6	NCI
76.	Nataraj	62	M	12	1	L	30	6	9	9	7	9	5	132	5	VaMCI
77.	Uma	50	F	10	1	R	30	7	12	12	13	13	5	90	8	NCI
78.	Moorthy	63	M	13	12	L	30	6	10	11	10	11	4	154	5	VaMCI

S.No	Name	Age	Sex	Education	Risk factors	Lateralisation	MMSE	Digit span	BNT	CNA	RAVLT - D	RAVLT - R	CDT	TMT	Territory	Diagnosi s
79.	Ramar	67	M	3	25	R	24	5	4	10	3	4	2	277	5	VaD
80.	Govindhan	75	M	7		R	24	4	9	9	2	7	2	281	6	VaD
81.	Paraman	0	M	10	236	L	27	4	9	10	8	12	5	254	6	VaMCI
82.	Angujam	56	F	6		R	30	6	10	11	10	11	5	100	8	NCI
83.	Tamilanban	71	M	4	136	L	21	3	7	11	5	9	4	195	5	VaD
84.	Saroja	64	F	4	15	L	30	7	10	10	10	11	5	95	5	NCI
85.	Selvam	54	M	7	123	L	29	6	11	12	5	13	3	276	6	VaMCI
86.	Panner	55	M	9	1	L	30	5	10	9	11	11	5	200	9	NCI
87.	Ravi	69	M	D	24	R	30	5	10	11	6	14	2	239	7	VaMCI
88.	Sivakami	50	F	5	1	R	29	7	11	11	11	11	4	110	5	NCI
89.	Rajakumari	51	F	7		L	25	5	12	12	13	11	5	120	6	NCI
90.	Kalaiyarasi	65	F	8	269	L	30	4	8	12	3	7	4	298	5	VaD
91.	Parthiban	68	M	5	18	R	30	6	6	9	4	11	5	129	8	VaMCI
92.	Kavi	65	M	6	19	L	30	9	7	8	9	11	5	211	9	VaMCI
93.	Alamelu	74	F	5	13	R	29	3	9	8	7	8	2	328	6	VaD
94.	Veramani	67	F	5	145	L	30	6	10	11	10	11	5	100	9	NCI
95.	Mathiyalagan	60	M	12	5	R	29	5	13	14	8	12	5	95	9	VaMCI
96.	Mani	56	M	11	237	R	25	5	12	12	10	10	5	105	6	NCI
97.	Veeran	63	M	6	137	L	24	5	7	6	2	6	3	401	4	VaD
98.	Rajathi	63	F	11	26	R	30	5	12	12	5	7	4	143	8	VaMCI
99.	Ezhil	48	F	0	25	L	30	6	11	17	8	12	5	135	3	VaMCI
100.	Ambalavanan	62	M	7	124	R	30	6	12	20	9	10	4	120	5	VaMCI

KEY TO MASTER CHART

SEX

M-male , F-female

EDUCATION

Number of completed years of education

D - Degree

RISK FACTORS

1-Hypertension, 2-Hyper Cholesterolemia, 3-Smoker, 4-Diabetes mellitus, 5-Previous TIA, 6-Previous stroke, 7-Previous AMI, 8-Previous angina, 9-Atrial fibrillation

LATERALISATION

R – Right, L- Left

TERRITORY

1-Left ICA, 2-Right ICA, 3-Left ACA, 4-Right ACA, 5-Left MCA, 6-Right MCA, 7-Left PCA, 8-Right PCA, 9-Vertebrobasilar